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SULPHONAMIDE THERAPY IN OCULAR DISEASES

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Introductory

The main idea of the work we have done is to find out the rationale of sulphonamide therapy in the treatment of infections of the anterior ocular tissues. For experimental purposes the sulpha drugs selected were: sulphanilamide, sulphapyridine, sulphathiazole, and sulphacetamide (Albucid). These are the drugs used mostly in the Ophthalmic Wards of K. G. Hospital, Lucknow.

For experimental purposes observations have been made on dogs of varying sizes, weights and breeds. The experiments have been extended to human subjects. Some patients have been given a clinical trial orally and locally in diseases of the cornea, conjunctiva, and aqueous.

Method of Assay

In this work the method of assay advocated by Dosle and Geiger has been selected for estimations of sulphonamide contents of blood and other ocular tissues.

Reagents required:—

1. 0·1 N.HCl.

2. 0·1 per cent $NaNO_2$ freshly prepared in distilled water.

3. Absolute alcohol.

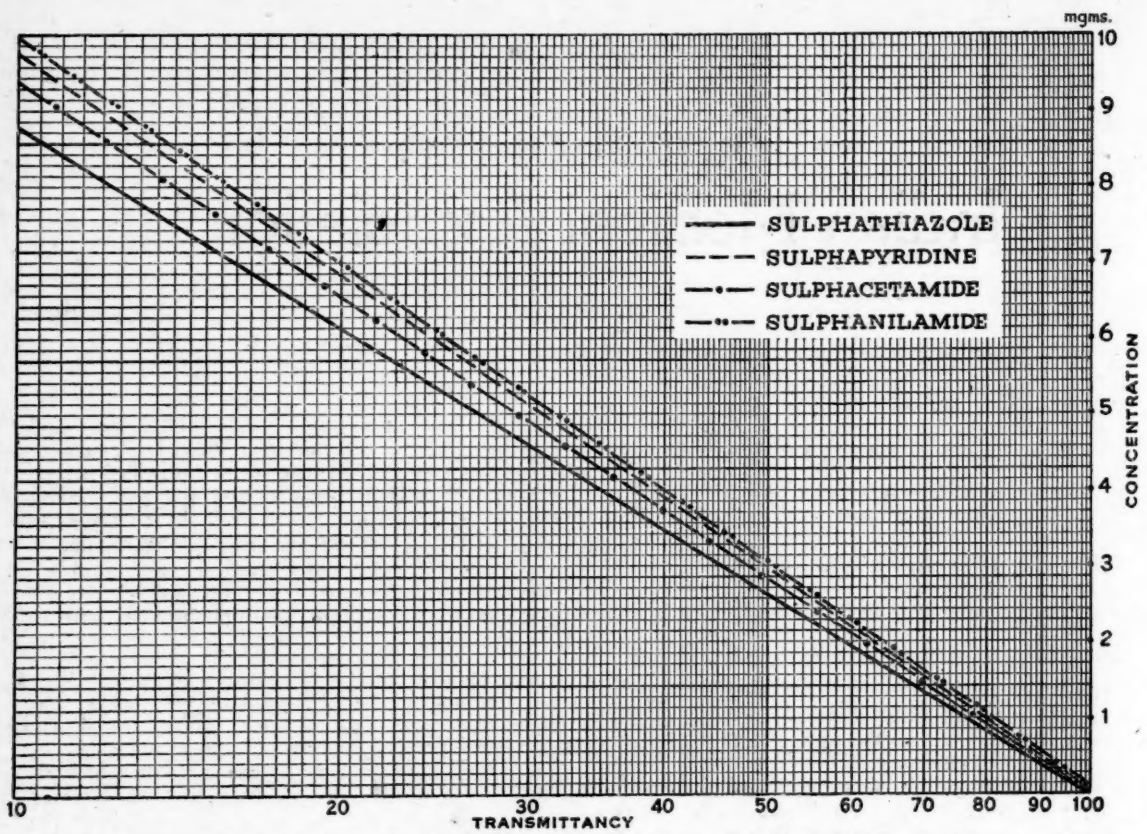
4. 0·5 per cent diphenylamine in 95 per cent alcohol.

5. Stock solutions of sulpha drugs varying from 0·5 to 10 per cent.

2 c.c. of venous blood is added slowly to 18 c.c. of absolute ethyl alcohol. This is allowed to stand for 15 minutes. After this it is filtered. 10 c.c. of the filtrate is treated with 5 c.c. of distilled water, 2 c.c. of 0·1 N.HCl, 1 c.c. of 0·1 per cent $NaNo_2$ solution. The total quantity is well shaken and after 5 minutes 1 c.c. of 0·5 per cent diphenylamine is added. This is allowed to stand for half an hour. Yellowish orange colour of various shades develop depending upon the degree of sulphonamide content.

As sulphonamide is not acetylated in dogs these were used for most of the experiments. They were weighed and the drug was suspended in milk and was administered by means of a stomach tube. In some it was not necessary to use it as they took the milk containing the drug themselves. They were starved overnight and the drug was administered at 7 a.m. next morning, the dose being 0·1 gm. per kilo of body weight. In order to identify the dogs, numbering was done on dogs' skin by Indian ink. Blood was collected from the femoral vein.

An instrument called Cenco-Sheard-Sanford Electrophotelometer has been used for comparison and estimation of sulphonamide content in the tissues. In short, the solutions of the four sulpha drugs already mentioned were prepared from 0·5 to 10 per cent very accurately and 0·1 c.c. of each solution was taken by means of a pipette which measured 2 drops. This was diluted with 10 c.c. of distilled water. The reagents for the estimation of sulphonamide were added as already described and the whole solution was transferred to the absorption cell of the photelometer. The photelometer was connected to a battery and after closing the iris diaphragm, the light and then the meter switch turned on. The fine adjustment control was then used to obtain a photelometer reading 100. It means 100 per cent transmission. Due to fatigue of the cell, adjustment of the photelometer reading to 100 was necessary from time to time. Then the cells containing the sulphonamide were placed on the adapters to get in the light path exactly. This reading was less than 100. The galvanometer readings were plotted on semi-logarithmic paper. A copy of



GRAPH 1—SHOWING THE CORRESPONDING PHOTELOMETER READINGS OF THE VARIOUS SULPHA GROUP OF DRUGS

it we got with the photelometer, and from it many copies were made. A straight line was obtained by joining the points. Thus the graphs were made for different sulpha drugs. (Graph 1.) Higher the concentration less the transmittancy. Care has been taken to clean the cells and remove the bubbles in the solution.

TABLE I—SHOWING THE CORRESPONDING PHOTELOMETER READINGS OF THE VARIOUS SULPHA GROUP OF DRUGS

Mgms.	*Sulph-anilamide*	*Sulpha-thiazole*	*Sulpha-pyridine*	*Sulph-acetamide*
10	10	..	..	..
9	14	10	10·3	11·3
8	17	12·5	15	16
7	20	16·5	18	19
6	25	20·7	22·5	24·5
5	30	27·5	28	30
4	38	33	35·2	36·5
3	50	44	47	47
2	60·2	59	63	61·5
1	81	78	80	80·2
0·5	90·4	90	92	89

DETERMINATION OF THE TIME SULPHA DRUGS STAY ON IN NORMAL HUMAN EYES WHEN APPLIED IN THE FORM OF DROPS AND OINTMENTS

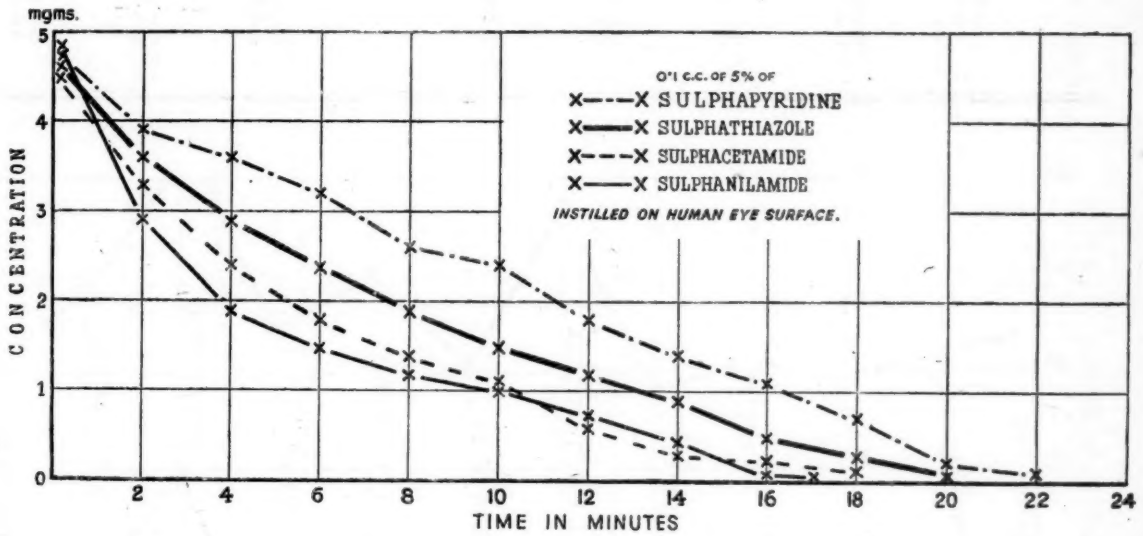
Human subjects were selected for this purpose specially the ward-boys and sweepers of K. G. Hospital. 0·1 c.c. of 5 per cent sulphonamide of each variety was dropped into the conjunctival sacs in different persons. Great care was taken in seeing that none of the medicines instilled goes out of the eye surface. This was ensured by making the patients lie flat after instillation, and the palpebral fissures were kept open by us. The experiments were carried on in the dark room to avoid blepharospasm and excessive lacrimation. Patients were allowed to close their eyes after a short interval of time *i.e.*, 3 to 4 minutes.

Because the lacrimal secretion differs in different persons, it was thought necessary to find out the exact amount of the drug present on the eye surface in the beginning just after the instillation. This gave the basal or floor value on which the further findings were based. After the instillation of the drug, eye bath filled with 10 c.c. of distilled water was applied on the patients' eye. Each patient was bent with the head forwards and downwards. After the eye-bath had been thoroughly stuck, the head was bent backwards.

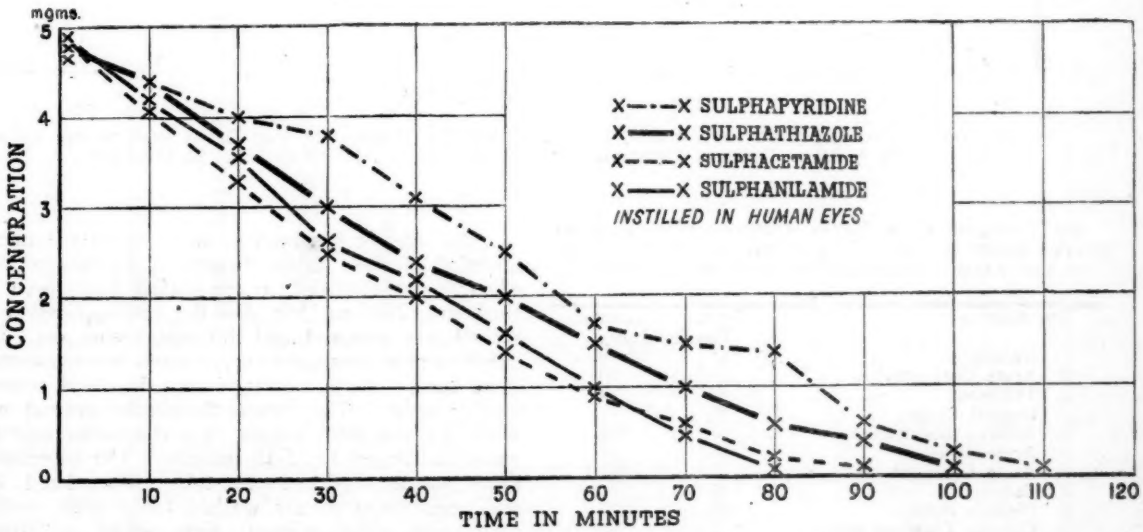
Patients were asked to open their eyes inside the water so that the latter might reach the fornices. Eyes were washed after 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 and 22 minutes. Findings were repeated in 10 sets of patients. The washed liquid was transferred to the test-tubes and reagents of sulphonamide estimation were added to them. Lighter colour was obtained as the time increased. The same procedure was adopted for other sulpha drugs. The amount of the sulphonamide content in the washings was read from the Photelometer Graphs already prepared for the sulpha drugs.

This was done in 25 sets of patients, and the average value found out.

Sulphonamide stays for different lengths of time in various diseases.



GRAPH 2—SHOWING THE CONCENTRATION OF THE SULPHA GROUP OF DRUGS, WHEN APPLIED AS DROPS, IN HUMAN EYES, AT VARIOUS TIME INTERVALS (TABLE II.)



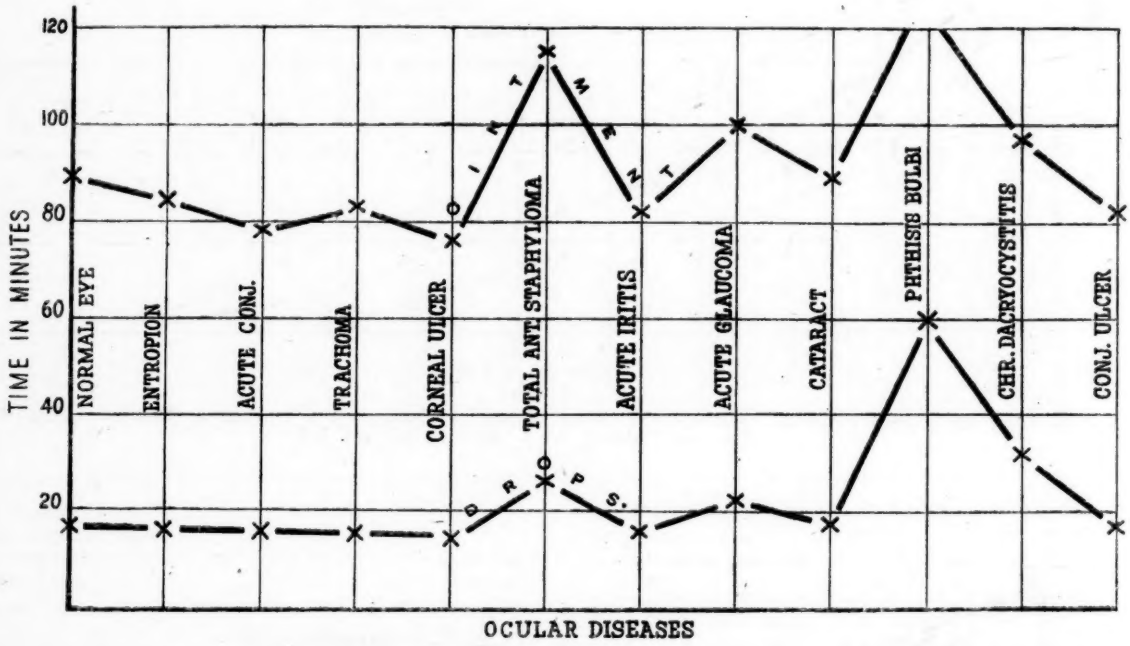
GRAPH 3—SHOWING THE CONCENTRATION OF THE SULPHA GROUP OF DRUGS, WHEN APPLIED AS OINTMENT, IN HUMAN EYES, AT VARIOUS TIME INTERVALS (TABLE III)

TABLE II—SHOWING THE CONCENTRATION OF SULPHA GROUP OF DRUGS AFTER DROPS INTO THE EYE, AT DIFFERENT TIME INTERVALS

Time in minutes	*Sulph-anilamide*	*Sulpha-thiazole*	*Sulpha-pyridine*	*Sulph-acetamide*
2	2·9	3·6	3·9	3·3
4	1·9	2·9	3·6	2·4
6	1·5	2·4	3·2	1·8
8	1·2	1·9	2·6	1·4
10	1·0	1·5	2·4	1·1
12	0·7	1·2	1·8	0·6
14	0·4	0·9	1·4	0·3
16	0·1	0·5	1·1	0·2
18	..	0·3	0·7	0·1
20	..	0·1	0·2	..
22	..	..	0·1	..

TABLE III—SHOWING THE CONCENTRATION OF SULPHA GROUP OF DRUGS, AFTER OINTMENTS ARE APPLIED TO THE EYE, AT DIFFERENT TIME INTERVALS

Time in minutes	*Sulph-anilamide*	*Sulpha-thiazole*	*Sulpha-pyridine*	*Sulph-acetamide*
10	4·2	4·4	4·4	4·1
20	3·6	3·7	4·0	3·3
30	2·6	3·0	3·8	2·5
40	2·2	2·4	3·1	2·0
50	1·6	2·0	2·5	1·4
60	1·0	1·5	1·7	0·9
70	0·5	1·0	1·5	0·6
80	0·1	0·6	1·4	0·2
90	..	0·4	0·6	0·1
100	..	0·1	0·3	..
110	..	..	0·1	..



GRAPH 4—SHOWING THE TIME IN MINUTES, DURING WHICH THE SULPHA GROUP OF DRUGS STAY IN THE NORMAL AND VARIOUS DISEASED CONDITIONS OF THE EYE, WHEN APPLIED AS DROPS OR OINTMENTS

TABLE IV—SHOWING THE TIME IN MINUTES DUKING WHICH THE SULPHA GROUP OF DRUGS STAY IN THE CORNEA IN NORMAL AND VARIOUS DISEASED CONDITIONS OF THE EYE

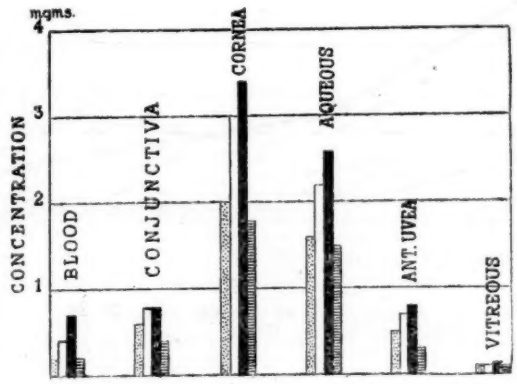
Eye-diseases	*Drops*	*Ointments*
	Time in minutes	
1. Normal	17	90
2. Acute Conjunctivitis ..	16	80
3. Trachoma	16	84
4. Corneal Ulcer	14	77
5. Anterior Staphyloma ..	26	116
6. Acute Iritis	16	82
7. Acute Glaucoma	22	100
8. Cataract	17	90
9. Phthisis Bulbi	60	175
10. Chronic Dacryocystitis ..	32	98
11. Conjunctival Ulcer ..	17	82
12. Entropion	17	85

An attempt has been made to assess the rate of diffusion of these drugs through the cornea of dogs when they are applied on eye surface every hour for six hours. Half an hour after the final application the eyeball was removed and different tissues cut. The sulphonamide content was estimated by transferring them one by one to mortars except the blood, vitreous and aqueous. They were thoroughly ground with sand in a minimum volume of trichloracetic acid and were centrifuged for 5-10 minutes. The supernatant liquid was decanted into a test-tube calibrated at 10 c.c., and precipitated matter washed twice with trichloracetic acid. The reagents were added as already directed and estimated by putting in light path of photelometer and graph.

It has been found that acetamide penetrates most and next in the order is sulphanilamide.

The sulphonamide content in the cornea is highest, next in order are aqueous and conjunctiva. The posterior ocular tissues contained only traces.

When ulcer was produced on the surface of the cornea, penetration was more than that through the normal cornea.



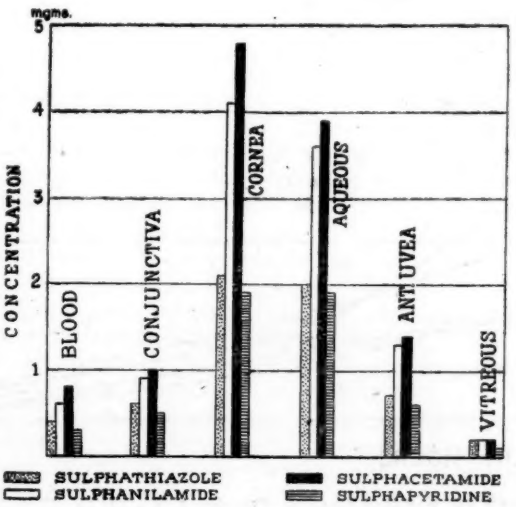


CHART (ABOVE) SHOWING THE CONCENTRATION OF VARIOUS SULPHA GROUP OF DRUGS IN DIFFERENT TISSUES OF THE EYE OF NORMAL DROPS WHEN APPLIED LOCALLY

CHART (BELOW) SHOWING THE CONCENTRATION OF VARIOUS SULPHA GROUP OF DRUGS IN DIFFERENT TISSUES OF THE EYE IN CORNEAL ULCER WHEN THESE DRUGS WERE APPLIED LOCALLY

TABLE V—TIME SHOWN IN MINUTES IN DOGS

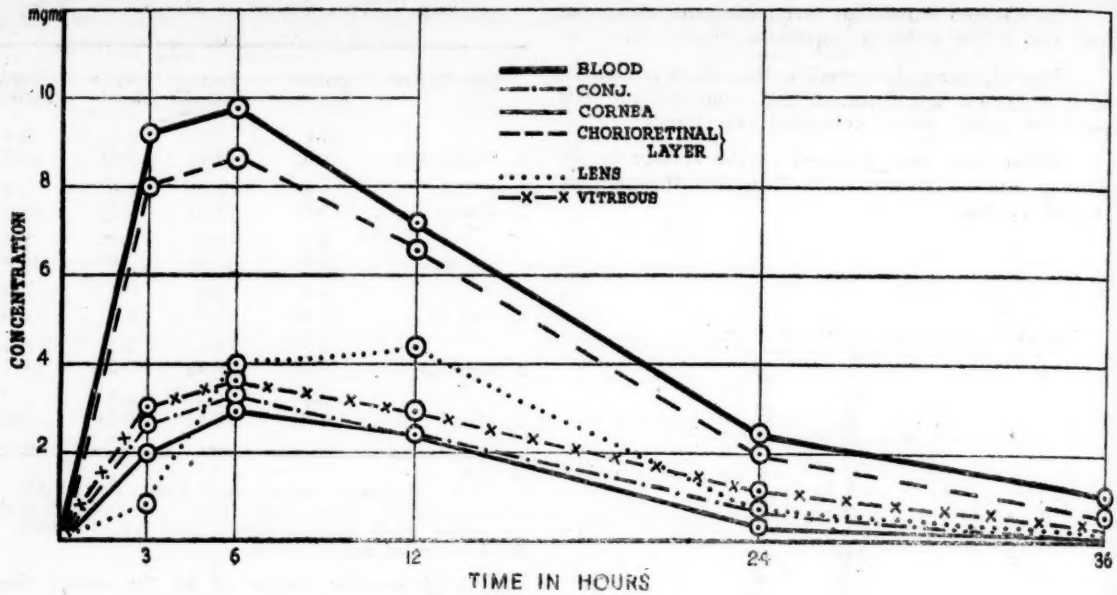
Eye Tissues	*Sulph-acetamide*	*Sulph-anilamide*	*Sulpha-thiazole*	*Sulpha-pyridine*
1. Conjunctiva ..	0·8 (1·0)	0·8 (0·9)	0·6 (0·6)	0·4 (0·5)
2. Cornea ..	3·4 (4·8)	3·0 (4·1)	2·0 (2·1)	1·8 (1·9)
3. Aqueous ..	2·6 (3·9)	2·2 (3·6)	1·6 (2·0)	1·5 (1·9)
4. Ant. Uvea ..	0·8 (1·4)	0·7 (1·3)	0·5 (0·7)	0·3 (0·6)
5. Vitreous ..	0·1 (0·2)	0·1 (0·2)	0·1 (0·2)	0·1 (0·1)
6. Blood ..	0·7 (0·8)	0·4 (0·6)	0·2 (0·4)	0·2 (0·3)

N.B.—The figures given above within the brackets are of the condition when corneal ulcer was produced in dogs by means of a Graefe's knife. The figures without the brackets are of normal cornea.

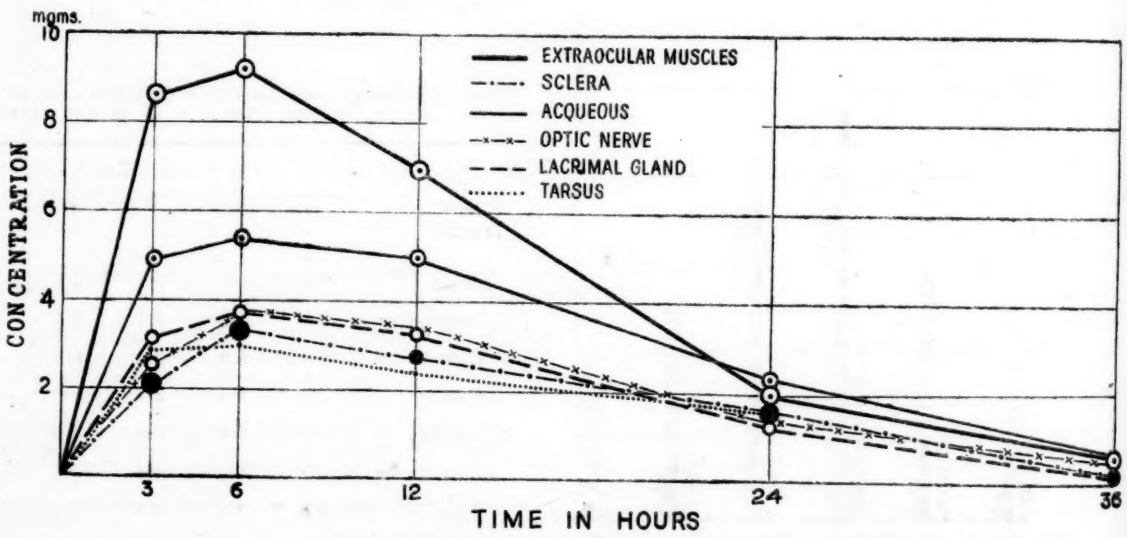
Sulphonamide content of all the ocular tissues has been estimated after administering the drug orally to dogs, the dosage being 0·1 gm. per kilo of body weight. Eyeballs were removed after 3, 6, 12, 24 and 36 hours after administration of the drug. The experiment was repeated in three sets of dogs and the average value taken.

TABLE VI—SHOWING THE AMOUNT OF SULPHONAMIDE IN THE VARIOUS OCULAR TISSUES AFTER 3, 6, 12, 24 AND 36 HOURS

Ocular Tissues	Time in Hours 3	6	12	24	36
1. Blood ..	9·2	9·8	7·2	2·1	0·8
2. Conjunctiva ..	2·6	3·2	2·6	0·6	..
3. Cornea ..	2·0	3·0	2·6	0·4	0·2
4. Sclera ..	2·2	3·4	2·7	1·5	0·3
5. Aqueous ..	4·9	5·7	5·0	2·0	0·4
6. Chorioretina	8·0	8·6	6·6	2·0	0·5
7. Lens ..	0·8	4·0	4·4	0·6	0·1
8. Vitreous ..	3·0	3·8	3·0	0·8	0·1
9. Optic nerve ..	2·6	3·6	3·4	1·4	0·2
10. Lacrimal gland	3·2	3·8	2·8	1·2	0·4
11. Extraocular muscles ..	8·6	9·2	7·0	2·0	0·6
12. Tarsus ..	2·8	3·0	2·4	1·6	0·3



GRAPH 5A—SHOWING THE SULPHONAMIDE CONTENT IN VARIOUS OCULAR TISSUES 3, 6, 12, 24 AND 36 HOURS AFTER ORAL ADMINISTRATION OF THE DRUG



GRAPH 5B—SHOWING THE SULPHONAMIDE CONTENT IN VARIOUS OCULAR TISSUES 3, 6, 12, 24 AND 36 HOURS AFTER ORAL ADMINISTRATION OF THE DRUG

All the tissues attain their maximum concentration at about the 6th hour.

To confirm the above findings in clinical practice Cibazol has been given by mouth in 10 patients and in another 10 patients sulphacetamide, due to its great power of penetration through the cornea, has been applied. In another 8 patients combined therapy was done. Cases were of acute conjunctivitis, trachoma and corneal ulcer. Sulphacetamide was applied in the form of 10 per cent ointment, every 3 hours in the day and every 6 hours in the night.

Results

Different Sulphonamides stay for different lengths of time on eye surface.

Table 7—Showing the Different Lengths of Time Different Sulphonamides Stay on Eye Surface

	Drops	*Ointments*
1. Sulphanilamide ..	17 minutes	1½ hour
2. Sulphathiazole ..	20 „	1 hr. & 40 min.
3. Sulphapyridine ..	22 „	1 hr. & 50 min.
4. Sulphacetamide ..	18 „	1½ hour

Sulphonamide stays for different lengths of time in various eye diseases. A table and graph have been presented.

After local administration the sulphonamide content in the cornea was highest and next in the order came the aqueous and conjunctiva. The posterior ocular tissues contained only traces.

The power of penetration through the cornea was found to be the greatest in sulphacetamide and next comes the sulphanilamide.

Distribution of sulphonamide in various ocular tissues is of interest. The muscles and chorioretinal layer contained the highest percentage of the drug closely approximating that found in blood. This is due to the fact that they are very vascular. The compound gets into the aqueous and the vitreous by dialysis from blood. The lens and cornea having no blood supply must secure its portion from surrounding media.

All the tissues attained their maximum concentration at about the 6th hour except the lens in which the peak was reached at about the 12th hour.

By far the most rapid concentration occurred till the 3rd hour. Those tissues attaining highest concentration lost it again most precipitately.

Cibazol produced marked relief in trachoma cases but no change was seen in corneal ulcer cases. Three out of 10 patients of acute conjunctivitis got cured and the rest of them did not show any sign of relief.

Cases with corneal ulcer, acute conjunctivitis and trachoma showed marked improvement and relief with sulphacetamide 10 per cent ointment application every 3 hours in the day and every 6 hours in the night. Eight cases of corneal ulcer out of 10 got cured in 5 days' time and the other 2 in 7 days. 6 cases of acute conjunctivitis got cured in 4 days' time and the rest in 6 days. 18 cases of trachoma were cured in about three weeks' time; 5 cases showed marked improvement and later recurrence; 2 cases did not show any sign of improvement whatsoever.

Reference

Dosle and Geiger—*J. Lab. Clin. Med.*, **23**:651, 1938.

USE OF STREPTOMYCIN IN TUBERCULOSIS*

A Review of 100 Cases

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Introductory

Streptomycin was discovered by Schatz Bugie and Waksman[1] about 1944 in their search for an antibiotic agent against the gram-negative bacteria. But perhaps more important than this discovery was its application by Feldman and Hinshaw[2] of the Mayo Clinic in the experimental tuberculosis in the highly susceptible guinea-pigs. Therapeutic effects in these animals were so striking that they were encouraged to begin clinical trials in human beings in the same year and the preliminary reports[3] of their observations were published in 1945. Since then extensive experimental and clinical trials have been undertaken by numerous investigators and a large volume of literature has already accumulated on the subject during the last three years.

Since the publication of the earlier clinical results in 1946, we had been trying to obtain this drug from U.S.A. as well as from the Government of India without success. In October 1947 an old lady, an advanced case of pulmonary tuberculosis, developed intense headache and other symptoms of meningism. At our suggestion her son, who is an air pilot, obtained through his American friends a small supply of streptomycin from America and that is how our first case was started. From November 1947 small supplies were made available through the courtesy of the newly established National Government of India. Since then the supply position has gradually improved and at present, in spite of the import restrictions, the drug is more easily available. In the beginning the price was also prohibitive and even now it is beyond the paying capacity of the average patient. For these reasons it has not been possible for us to try the drug very methodically in selected groups of cases. As a matter of fact, we gave streptomycin wherever the patients failed to improve under recognised methods of treatment provided they could afford the expenses involved.

Clinical Material

We shall present in this paper the results of clinical studies on streptomycin carried out at the Jadabpur Tuberculosis Hospital for a period of one year—from October 1947 to October 1948. Altogether 120 cases have been treated. In ten cases the treatment has only recently been started and they are left out of this study. Another group of 10 cases received a short course (less than 10 gms.) and are considered separately. This leaves us with 100 cases which have been included in the general survey.

*Read at the 6th Tuberculosis Workers' Conference, Calcutta, 1948.

Age and Sex

Out of 110 patients 85 were men and 25 women. They were mostly young adults although extremes of life were also represented. The oldest was a man of 54 and the youngest a boy of 5.

Table I—Age & Sex

Age groups	*Men*	*Women*	*Total*
Below 15 yrs.	2	nil	2
15—20 „	15	3	18
21—30 „	36	17	53
31—40 „	22	3	25
41—50 „	7	2	9
Over 50 „	3	nil	3
Total	85	25	110

Preparation used: Mode of Action: Resistance to Streptomycin

Most of the cases in our series received injections of streptomycin sulphate of different makes (Lilly, Warner, Upjohn, Pfizer, Parke Davis, Cutter). In the initial stages we used streptomycin hydrochloride (Squibb, Merck) but the injections were so painful that we were forced to stop its use. The same remarks apply to one brand of sulphate (Cutter). Hinshaw and others[4] claim that there is no particular advantage in using either salt. The pain is perhaps due to impurities present and will disappear with the improvement of the technique of manufacture.

Although it has been established that streptomycin has a retardant action on the growth and multiplication of Mycobacterium tuberculosis both *in vitro* and *in vivo*, its mode of action is not yet fully understood. It certainly abolishes the toxæmia within a few days of the institution of treatment. But the greatest drawback to its extensive use is the development of resistance of the bacillus to streptomycin. It has been reported by different observers[5] that in 60 to 70 per cent of cases the originally streptomycin-sensitive bacilli develop this resistance within 60 to 120 days. The experiments made so far indicate that this acquired resistance to streptomycin is irrevocable. It is unfortunate that we could not obtain materials for testing the sensitivity during the course of this study.

Dosage: Technique of Administration

Keeping in view the development of resistance the earlier workers recommended a heavier dose while the bacilli were still sensitive. They suggested a daily dose of 3 gms. given intramuscularly at 4 hourly intervals. Toxic manifestations observed in these cases made them revise their opinion. The Veterans Administration and the Army and Navy of the U.S.A.[5] who initiated a systematic study of this drug in 543 cases of tuberculosis of all types used 1·8 gms. per day (0·3 gms. every four hours). Hinshaw and Feldman[4] in their article on the technique of streptomycin therapy published in November, 1947 recommended 1·0 gm. per day for 'less critical types' and 1·5 to 2·0 gms. per day for the 'most serious critical types' of tuberculosis. They suggested that injections should be given at 6 hourly intervals.

In our series we aimed at achieving the maximum clinical improvement with the minimum of injury to the patient. In many cases the scarcity of the drug and the financial condition of the patient were also taken into consideration. In our earlier cases we tried to maintain a daily dosage of 2·0 gms. a day (0·25 gms. every 6 hours) but owing to severe local reactions we could not continue it. Gradually we reduced the dose to 1·0 gm. a day (0·5 gm. every 12 hours) and in weak and emaciated cases to 0·5 gm. once a day. This reduction in dosage, while maintaining the standard of improvement, cut down the reactions to a minimum. Our plan of dosage adopted at different times together with the number of patients is given in the table below:

Table II—Plan of Dosage

	Plan of dosage	*No. of cases*
(*i*)	0·5 gm. every 6 hrs. followed by 0·5 gm. twice daily	2
(*ii*)	1·0 gm. twice daily till abolition of toxæmia followed by 0·5 gm. twice daily	4
(*iii*)	0·5 gm. twice daily till abolition of toxæmia followed by 0·5 gm. once daily ..	26
(*iv*)	0·5 gm. twice daily throughout ..	40
(*v*)	0·5 gm. once daily	34
(*vi*)	Instillation only into the pleural space and sinuses	4
	Total ..	110

The injections were given intramuscularly into gluteus or the deltoid. 1 gm. of the drug was dissolved in 4 c.c. of Normal Saline or sterile distilled water (250 mgm. per c.c.) and half portion was injected twice or once a day as the case may be. The dissolved solution, transparent and almost colourless in the beginning, turns on keeping into a light to deep brown colour. When the injections were first started they were so painful that we had to mix each dose with an equal quantity of 1 per cent procaine solution before injection. The products that we are now using are almost painless and the use of procaine has been discontinued in all but a few sensitive patients.

Total Dosage: Duration of Treatment: Multiple and Interrupted Courses

10 cases in the series were given short courses. The average quantity for this group is 5·2 gms. and the average duration of treatment 11 days.

Our figures for the remaining 100 cases are as follows:—

Table III—Dosage & Duration of Treatment

1.	Average amount of streptomycin per patient (Maximum 135 gms.: Minimum 12 gms.)	44·27 gms.
2.	Average duration of treatment ..	59·11 days
3.	More than one course for relapse of symptoms	11 cases
4.	Course interrupted for various reasons ..	25 „
5.	Average duration of interruption ..	13·1 days

Our usual procedure was to give a 2-4 months' course of 60 gms. to each patient unless severe toxic reactions or financial reasons called for an earlier termination. After 60 gms. the case was reviewed and a further 30 gms. were given wherever necessary. In 5 patients the course was terminated after 20 gms. as being totally ineffective.

Of the 11 patients who received multiple courses for recurrence of symptoms, 9 had two courses and 2 had three at intervals varying between 1 and 4 months. In 8 out of 11 cases (72·7 per cent) the second course was effective in checking the symptoms. In 3 others it failed.

The course had to be interrupted in 25 patients for periods varying from 2 to 20 days, the average duration being 13·1 days. The reasons were:—

Financial	13
Reactions	7
Hæmoptysis	5
TOTAL ..	25

TOXIC MANIFESTATIONS

A variety of toxic manifestations have been reported by workers on streptomycin. Hinshaw and Mcdermott reporting to the Committee on chemotherapeutics and other agents under the National Research Council of the U.S.A.[6] mentioned the following group of toxic symptoms:—Local irritation, histamine like reaction, sensitisation reactions, neurologic disturbances and disturbances of the eighth nerve. The Streptomycin Committee of the Veterans Administration reporting toxicity in 223 cases of pulmonary tuberculosis[7] found among other manifestations—Vertigo (91·5 per cent) eosinophilia (69·5 per cent), urinary casts (67·3 per cent), albuminuria (20·2 per cent), tinnitus (46·8 per cent) dermatitis (19·8 per cent) and nausea and vomiting (10 per cent). The toxic manifestations observed in our series are given in the following table:

TABLE IV—TOXIC MANIFESTATIONS

Systemic Manifestations	*Quantity of streptomycin before appearance*					*Incidence in 100 patients*
	Upto 10 gms.	10-20 gms.	20-40 gms.	40-60 gms.	Over 60 gms.	Total per cent.
Vertigo ..	5	9	17	7	2	40
Nausea & vomiting (persistent) ..	3	2	1	..	1	7
Headaches & Insomnia ..	1	2	3	..	1	7
Fever with rigor ..	2	..	2	2	..	6
Anæmia		1	1	..	3	5
Ear Symptoms (Tinnitus: Partial Deafness)		..	..	3	2	5
Skin Rash		..	..	..	4	4
Salivation		..	1	..	2	3
Burning sensation all over the body ..	2	1	..	..	..	3
Dim Vision		..	..	..	1	1

Local manifestations—Pain at the site of injection was very severe with streptomycin hydrochlor (Squibb). 16 patients complained of pain and tingling. In one case there was actual necrosis and ulceration. The purified drugs which are now available do not cause local pains. Urticarial rash appeared at the site of the injection in two cases. These were seen soon after the injection and disappeared in three hours.

Vertigo was the commonest symptom (40 per cent). In some cases it was present from the beginning although in the majority it appeared after the administration of 20 gms. In 7 cases it was severe enough to cause interruption of the treatment for a few days. In others the patients soon adapted themselves without much difficulty. In most cases vertigo disappeared in 2-3 weeks from the cessation of treatment.

Anæmia, ear symptoms, skin rashes, salivation and eye symptoms developed in most cases (15 out of 18) when about 60 gms. or more were administered. In 2 cases the anæmia was so severe as to require repeated blood transfusions.

Partial deafness was observed in two cases. It improved considerably in about 3 months.

Skin rashes were of the maculopapular variety scattered all over the body. The condition was associated with pruritus and oozing and persisted throughout the course. In 2 of the 4 cases healing of the rashes was followed by pigmentation.

Allergic skin rashes in the fingers was found in one of our male nurses who handled streptomycin. These appeared as vesicular rashes on the contiguous surfaces of the right index and middle fingers which came into contact with streptomycin solution. There was a lot of itching and exudation suggesting eczema of the fingers. As the condition became worse, he was advised to wear gloves while making the streptomycin solution. The condition took about 6 months to subside and a little roughness of the skin with slight itching persists till to-day (10 months). This case was similar to six cases of sensitivity recently reported by Rauchwerger and others.[11]

Salivation is of special interest. We do not find it mentioned in the literature published so far. In 2 out of the three cases salivation appeared after completion of the 60 gms. course and persisted for 3 months. In the third case it appeared after 20 gms. and continued for three days.

In the group that received short cuorse (average 5·2 gms.) one case showed signs of intolerance. With every injection (0·5 gm.) he got severe chills and the temperature shot up from 98·4°F. to 104°F. Six injections at varying intervals and using different preparations produced the same results. The treatment was abandoned.

We have also studied the toxic manifestations in relation to age and sex. Nothing particular came out of this study except the fact that all patients over 40 numbering twelve had reactions of some sort.

Albuminuria was not present in our series. Eosinophilia occurred in 48·9 per cent of the cases studied. The mildness of reactions in our series as compared to published figures is probably due to smaller doses, greater intervals and shorter courses.

Results of Treatment

We shall now proceed to analyse the results of treatment. For this purpose we have divided our cases into groups and the overall picture of the results is given in Table V.

Bilateral pulmonary tuberculosis—Group 1 consisted of 72 cases of far advanced pulmonary tuberculosis with toxæmia. We have classified them into four groups to bring into prominence the discrepancy in results according to the nature of the complication. The number of cases where abdominal, laryngeal and other complications existed (Group 1—B, C and D) was 34 out of 72. Contrary to what one might expect, the results for these groups were definitely superior to the results for the group where no such complications existed (Group 1A—38 cases). The percentage of quiescent cases is 15·8 in Group 1A whereas it was as high as 30 in Group B, C and D put together. This trend is also reflected in the bad results. In Group 1A, 36·8 per cent did not improve and 5·3 per cent died. In Groups B, C, and D only 3 out of 34 cases (9 per cent) did not improve and there were no deaths.

This discrepancy tends to suggest that where toxæmia in pulmonary tuberculosis is due to enteritis and laryngitis, streptomycin by healing the sources of toxæmia also helps in the healing of lung disease but where the toxæmia is due to some factor hitherto unknown streptomycin is at best a palliative.

Streptomycin in thoracoplasty—Streptomycin was also found to be a very valuable adjunct to thoracoplasty. In 16 cases of the collapse therapy group 13 were cases of thoracoplasty. Analysis of these 13 cases shows that streptomycin was used

(*i*) to reduce the fever and improve the general condition before the operation—2 cases—both successful,

(*ii*) to check fresh contralateral spread after the operation—3 cases—2 successful,

(*iii*) to check tracheobronchitis with positive sputum following thoracoplasty—5 cases—all successful,

(*iv*) to check fever and abdominal symptoms following thoracoplasty—one case—successful.

(*v*) as a routine pre- and post-operative treatment to prevent complications—2 cases—successful.

Table V—Results of Treatment

Groups	*No. of cases*	*Good results*			*Bad results*	
		Quiescent	Much improved	Improved	No change	Died
1. Bilateral pulmonary tuberculosis (including non-pulmonary complications) where the recognised methods of treatment have failed to check the disease:						
A. With high fever and low general condition (No other complications)	38	6 (15·8%)	7 (18·4%)	9 (23·7%)	14 (36·8%)	2 (5·3%)
B. With abdominal symptoms: pain, tenderness, diarrhœa, anorexia and loss of appetite ..	19	5 (26·3%)	5 (26·3%)	9 (42·1%)	1 (5·3%)	..
C. With laryngeal symptoms: Loss or huskiness of voice and/or dysphagia were present ..	7	2 (28·6%)	2 (28·6%)	2 (28·6%)	1 (14·2%)	..
D. With glandular, meningeal and a combination of other complications	8	3 (37·5%)	3 (37·5%)	1 (12·5%)	1 (12·5%)	..
2. Unilateral pulmonary tuberculosis having collapse therapy. Streptomycin used as adjunct to collapse therapy (Thoracoplasty 13: A.P. & P.P.—3) ..	16	7 (43·7%)	6 (37·5%)	3 (18·8%)	..	..
3. Empyema complicating A.P. treatment ..	7	..	3 (42·8%)	..	4 (57·2%)	..
4. Non-pulmonary tuberculosis:						
Spinal caries 2						
Multiple cold abscess breaking down into ulcers 1						
Cervical and mesenteric lymphadenitis .. 1						
Sinus in the chest wall following plasty .. 1						
	5	2 (40%)	..	2 (40%)	1 (20%)	..
Total ..	100	25 (25%)	26 (26%)	25 (25%)	22 (22%)	2 (2%)

Non-pulmonary tuberculosis—The results in 2 cases of spinal caries was disappointing, one case with discharging sinuses was treated with 120 gms. with no results.

Very good results were obtained in one case of multiple cold abscesses over the chest and back which in spite of repeated aspirations broke down into ulcers, one of which was about 4″×3″. With the initiation of treatment the temperature came down from 101·4 to 98·4°F. in 5 days and the ulcers rapidly healed. Nothing but a few puckered scars remained after two

months. X'ray showed caries of the 5th to 8th ribs which also improved.

A case of sinus in the chest wall persisting for more than a year after thoracoplasty healed with local instillation.

There was a boy of 5 showing cervical and mesenteric lymphadenitis. The glands became smaller and the fever was reduced in the beginning but the improvement was not maintained.

Empyema—Of the 7 cases in our series

(*i*) 3 received intrapleural instillations only (0·1 to 0·2 gm. in 2 c.c. of Normal Saline daily) and

(*ii*) 4 received intramuscular injection (combined in 2 cases with intrapleural instillation).

Out of 7 cases three showed considerable improvement in the general health but the size of empyema cavity did not show any change. 2 cases ultimately came up for thoracoplasty.

Overall results—Our overall end-results show varying degrees of improvement in 76 per cent of cases. The period of observation after the termination of the therapy has not been sufficiently long. The good results indicated above were judged on the status of the patient soon after the termination of the treatment.

Published results on streptomycin are mostly based on a small number of cases and even where a large number of cases have been collected (*Ref.* 5-543 cases and *Ref.* 6-1000 cases) only general impressions are given.

Fisher, Tingey and Wallace[8] have tabulated the results of 100 cases of pulmonary tuberculosis which show 'excellent' results in 51 per cent, 'mediocre' results in 37 per cent and 'no improvement' in 12 per cent. In a study by the Veterans Administration of 223 cases about 85 per cent were judged to have improved on the basis of radiology and clinical observations. Our results, considering the preponderence of far advanced cases, compare favourably with these results.

Clinical Observations: Effects on Signs & Symptoms: Laboratory Tests

From a consideration of the overall picture we shall now proceed to examine the effect of the drug on the signs and symptoms. The results of clinical observations are presented in a tabular form.

Table VI—Effect on Temperature

Total No. of cases considered	*Afebrile before treatment*	*Febrile before treatment*		*Results after treatment* Rendered afebrile	Fever reduced	No change or worse
100	4	Upto 100°F	24	60	12	24
		„ 102°F	53	(62·5%)	(12·5%)	(25·0%)
		Over 102°F	19			
		Total ..	96			

The reduction of fever was one of the first signs of improvement and occurred in 75 per cent. In most cases it became apparent during the first 3 or 4 days of treatment although it might take some time for it to settle down to normal as would appear from Table VII.

Table VII—Time taken for the Fever to Subside (Analysis of 60 Cases)

	No. of cases	*Per cent*
In less than 10 days	26	43·3
In 11 to 20 „	10	16·7
„ 21 to 30 „	11	18·3
„ 31 to 60 „	10	16·7
„ 61 to 90 „	3	5·0
Average 22·5 days	60	100·0

Table VIII—Effect on the Amount of Sputum

No. of cases in the series	*No sputum before treatment*	*Having sputum before treatment*	*Results after treatment* Disappeared	Appreciably reduced	No change
100	7	Scanty to 1 cup or more 93 cases	33 (35·5%)	29 (31·2%)	31 (33·3%)

In 66·7% cases the sputum disappeared or was appreciably reduced in quantity.

Table IX—Effect on Haemoptysis

No. of cases in the series	*Hæmoptysis before treatment*		*After treatment* Checked	Unchecked
100	Recurrent ..	10	3	21 (60% of hæmoptysis cases)
	Occasional ..	25	11	
	Total ..	35	14 (40% of hæmoptysis cases)	
	35%			

The cases in which hæmoptysis was checked were mostly those treated with collapse therapy. Streptomycin appears to have no effect whatsoever on hæmoptysis.

Improved appetite was a noticeable feature of the majority of cases. Ascites was present in 4 cases. In 2 the fluid was absorbed and in the other 2 it remained unchanged. Two had lumps in the right iliac fossa which disappeared after treatment.

Most of these may be assumed to be cases of tuberculous enteritis although no detailed study was made by radiography. The examination of the stool of these cases did not reveal any ova or parasites to account for the symptoms. Before the discovery of streptomycin we had no remedy which proved so successful.

The solitary case where improvement did not occur was treated with streptomycin spray only. The results in this group as in the abdominal group are very gratifying. Laryngoscopic examination made in 2 cases before and after treatment showed complete healing of the ulcers. No other known treatment has been so successful.

TABLE X—EFFECT ON ABDOMINAL SYMPTOMS

No. of cases in the series	*Symptoms present before treatment*	*After treatment*		*Average period in which improvement occurred*
		Symptoms completely checked	Improved	
100	Loss of appetite, abdominal pain, tenderness, anorexia and diarrhœa Mild .. 9 cases Severe .. 7 „ Total .. 16 „ (16%)	14 (87·5%) of 16 cases	2 (12·5%) of 16 cases	12 days.

TABLE XI—EFFECT ON LARYNGEAL SYMPTOMS

No. of cases in the series	*Symptoms present before treatment*	*Result of treatment*		
		Voice clear	Voice greatly improved. Dysphagia relieved	No change
100	Voice husky or completely lost 15 cases (15%) Dysphagia in 3 cases	4 (26·6%)	10 (66·6%)	1 (7·8%)

TABLE XII—EFFECT ON TRACHEOBRONCHIAL SYMPTOMS
(THORACOPLASTY CASES ONLY)

No. of cases considered	*Tracheobronchial symptoms present*	*Result of treatment*
13	Excessive cough with moderate expectoration often accompanied by wheezing: sputum T.B. positive 5 cases (38·5%)	Disappearance of cough and sputum: sputum converted to negative 5 cases (100%)

5 of our 13 cases of thoracoplasty suffered from these tracheobronchial symptoms although no demonstrable cavity was present. Streptomycin helped in the arrest of disease in all cases.

One of our colleagues, Dr. K. S. Ray (Jr.)[9] studied the effect of streptomycin in 12 cases of endobronchial tuberculosis diagnosed by bronchoscopy at the Trudeau Sanatorium, U.S.A. He also found that streptomycin was of definite value in reducing cough and expectoration and that the sputum was converted in most of the cases.

TABLE XIII—EFFECT ON LYMPHADENITIS

Total No. in the series	*Lymphadenitis present before treatment*	*Result of treatment*
100	Cervical .. 3 cases Abdominal .. 3 „ Both cervical & abdominal .. 2 „ Total .. 8 „ (8%)	In all cases the glands became smaller and harder but did not return to normal.

The effect on glands were temporary and palliative in 6 out of 8 cases. In 2 cases the glands are retrogressing during the 3 months of observation.

TABLE XIV—EFFECT ON SINUS, ULCER, THROMBOPHLEBITIS

Symptoms	*No. of cases*	*Mode of administration*		*Results of treatment*
Fistula-in-ano ..	5	Intramuscular ..	2	
		Topical ..	3	
		(after operation)		All healed
Ulcers on the palate, tongue, and tonsil ..	3	Intramuscular ..	1	2 healed,
		Local ..	2	1 improved
Cutaneous sinuses & ulcer	4	Local		All healed
Progressing thrombophlebitis of the veins of both arms not affected by penicillin and anti-coagulant therapy	1	Intramuscular		Checked

TABLE XV—SPUTUM CONVERSION

Total No. of cases in the series	*T.B. absent before treatment*	*T.B. present before treatment*	*Sputum converted to negative* on termination of treatment	in 3 months from termination	*T.B. present after 3 months*
100	46 (46·0%)	54 (54·0%)	26 (48·1% of positive cases)	30 (50·5% of positive cases)	24 (44·5%)

The rate of conversion in the American literature,[5, 7] is from 32 to 43 per cent. Somewhat better results in our series are perhaps due to our different standard of judging the end results. We considered the sputum negative if 6 consecutive smear examinations spread over 3 months did not reveal any mycobacteria tuberculosis.

It was possible to study the blood changes in 45 cases before and after treatment. The results observed are given in the tables below:

TABLE XVI—R.B.C., HEMOGLOBIN AND S.R. TABLE

Before treatment	*No. of cases*	*After treatment* Increased (over 10%)	No change	Reduced (over 10%)
R.B.C.				
3-4 million per c.m.m.	41			
over 4 „ „ „ ..	4			
	45	6 (13·4%)	27 (60·0%)	12 (26·6%)
Hæmoglobin (Tallqvist)				
upto 50 per cent. ..	3			
50 to 60 „ „ ..	36			
over 60 „ „ ..	6			
	45	20 (44·4%)	19 (42·2%)	6 (13·4%)
S.R. (Westergren 1 hr.)				
15 to 30 m.m. ..	1			
31 to 50 m.m. ..	6			
over 50 m.m. ..	28			
	35	.. ..	27 (77·1%)	8 (22·9%)

Our results do not corroborate the improvement in blood condition and reduction in sedimentation rate reported by other observers. Whereas there was some improvement in the hæmoglobin percentage, the number of R.B.C.'s actually declined in about 26·6 per cent cases. In this connection mention may be made of three cases of toxic aplastic anæmia which have been reported in the current literature.[13, 14] In the sedimentation rate also, there is only a small reduction but none of the cases treated showed a normal rate (Below 15 m.m.—Westergren—one hour).

TABLE XVII—LEUCOCYTES: POLYMORPHS

Before treatment	*No. of cases*	*After treatment* Increased (over 20%)	No appreciable change	Decreased (over 20%)
Leucocytes (Total)				
upto 6000 per c.mm.	3			
6000 to 8000 „ ..	18	10 (22·3%)	12 (26·6%)	23 (51·1%)
8000 to 10000 „ ..	12			
over 10000 „ ..	12			
	45			
Polymorphs				
60 to 70% ..	8	7 (15·6%)	18 (40·0%)	20 (44·4%)
71 „ 80% ..	20			
over 80% ..	17			
	45			

There was decrease in the leucocytes in 23 cases (51·1 per cent). In 11 cases the count fell below 6000/c.mm. but the proportion of granulocytes was not seriously affected.

TABLE XVIII—EOSINOPHILS

Before treatment	*No. of cases*	*After treatment* Increased (over 5%)	No appreciable change	Decreased (about 5%)
Eosinophils upto 5% ..	35			
5 to 10% ..	8	22 (48·9%)	16 (35·6%)	7 (15·5%)
over 10% ..	2			
	45			Total absence of eosinophils in 5 cases

Eosinophilia was observed in 48·9 per cent. In 5 cases the differential count ranged from 24 per cent to 32 per cent. In no case did it exceed 32 per cent.

On the other hand eosinophils were reduced in 7 cases (15·5 per cent) in 5 of whom there was complete eosinopenia.

RADIOGRAPHIC CHANGES WITH STREPTOMYCIN

Abolition of toxæmia and a feeling of well-being marks only the beginning of the healing process in tuberculosis. We have observed this in the case of collapse therapy. In streptomycin treatment also the abolition of toxæmia does not correspond to immediate healing of lesion, and signs of retrogression in the skiagram continue to operate after the cessation of treatment. We are giving below the changes observed by us at the termination of the treatment. Owing to scarcity of the x-ray films during the greater part of this study, we could not collect the data of all cases.

TABLE XIX—CHANGES IN X-RAY FILM

	No. of cases	*After treatment* Almost cleared up	Much improved	No improvement
1. Confluent exudative infiltration ..	6	3 (50·0%)	1 (16·6%)	2 (33·4%)
2. Disseminated mixed infiltration with predominance of exudative infiltration ..	44	12 (27·3%)	14 (31·8%)	18 (40·0%)
3. Disseminated infiltration predominantly productive ..	5	..	3 (60·0%)	2 (40·0%)
Total ..	55	14 (27·3%)	18 (32·7%)	22 (40·0%)

TABLE XX—CHANGES IN CAVITIES

Present before treatment	*No. of cases*	*After treatment* Reduced in size	No change	*More prominent after absorption of exudate*
Large (Over 4 c.m)	5			
Medium ..	12			
Multiple small ..	8			
	25	8 (32·0%)	12 (48·0%)	5 (20·0%)
(45·5%) out of 55 cases.				

TABLE XXI—SUMMARY OF X-RAY FINDINGS

No. of cases considere	*Favourable*	*Stationary*	*Worse*
55	33 (60·0%)	17 (30·9%)	5 (9·1%)

The number of cases of the confluent and productive type of disease was so small that they do not bear any comparison to the predominantly exudative group.

The effect of streptomycin in clearing up the exudative infiltrations were very striking in 15 out of 55 cases (27·3%) and absorption to a varying degree occurred in 60%. Cavities were reduced in size in 32%.

Comparative Study of the Clinical and Laboratory Observations and Changes in the X-ray Film

We shall compare our results of 100 cases with the results of 223 cases studied by Streptomycin Committee of the Army, Navy and Veteran Administration of the U.S.A.[7] Only items for which comparable figures are available have been included in this list.

Table XXII—Comparative Study

Items for comparison	*Jadabpur Series 100 cases*	*American series 223 cases*
Temperature decrease ..	75 per cent	73·1 per cent.
Sputum decrease ..	66·7 „ „	79·8 „ „
S.R. decrease ..	22·9 „ „	51·1 „ „
Sputum conversion ..	55·5 „ „	43·0 „ „
Eosinophilia ..	48·9 „ „	69·5 „ „
X-Ray changes:		
Exudative lesions regression ..	60·0 „ „	84·7 „ „
Cavities smaller or closed ..	32·0 „ „	62·6 „ „

The effect on temperature in both series is about the same. Our results for sedimentation rate-decrease and eosinophilia are definitely lower than the American figure. As a matter of fact we did not have a single case where S.R. came down to normal in spite of improvement in other respects.

In regard to sputum our figures show a lower rate in sputum decrease but a higher rate in the conversion of positive sputum into the negative. The difference may be due to different standard of judging the end-results.

Our results for x-ray changes are not as satisfactory as the American results.

Discussion

To evaluate the results of any treatment it is useful to have two approximately parallel groups of cases. Other conditions remaining the same, one group should receive the new treatment so that the end results may be compared. Guess work based on clinical experience as to what have happened to a particular group if untreated is at best an inaccurate criterion. A study of 2 such parallel groups with and without streptomycin "exerts a beneficial effect in excess of what may be obtained by bed-rest as the sole form of treatment."

All observers agree that the abolition of toxæmia is very rapid and very striking. Within a week from the initiation of the treatment the fever and cough are reduced, the appetite improves and there is a general feeling of well-being although some of these results may not last till the end.

Another factor that struck us was the uniformly good results obtained in cases treated with as small a dose as 0·5 gm. once daily.

How does streptomycin act? That question has not been fully answered. The bacteriostatic action of the drug has been established but that does not explain all the results. It does not appear to possess any bactericidal action. We have not met with any reactions which might be compatible with the sudden killing of a large number of bacteria. Besides, the improvement is not accompanied by or proportionate to the number of bacilli in the sputum.

Is the abolition of toxæmia due to its antitoxic action? It may be one of the possible explanations but we do not yet know the mechanism by which streptomycin neutralises or absorbs the tuberculous toxins.

Good results obtained with small doses at 24 hourly intervals suggest that maintenance of blood concentration level sufficient to exert bacteriostatic action is not essential. An explanation has been offered by Feldman and others[15] that streptomycin sticks to the tissues and acid-fast organisms and continues to act even when the drug has disappeared from the blood. If that be so, a good deal more work is needed to find the optimum dosage and interval.

Streptomycin resistance developed by the organisms also requires further study. Will the small doses make the organisms more resistant and frustate the object of treatment? Is the clinical improvement dependent upon sensitivity or resistance of the bacteria? These questions must be answered.

We have indicated some of the thoughts which crossed our mind while studying the results. More extended work—clinical, radiological, bacteriological and biochemical—and higher standards of evaluation of results are necessary before we can draw any conclusions.

Summary and Conclusion

We shall conclude the paper by giving a brief summary of our observation and experience:

1. The paper is based on a study of streptomycin treatment in 100 cases at Jadabpur Tuberculosis Hospital from October 1947 to October 1948.

2. Small doses of streptomycin are well tolerated, and the results are quite encouraging. Even 0·5 gm. once daily was found sufficient for thin and emaciated patients.

3. The average quantity of streptomycin given per patient was 44·27 gms. and the average duration of treatment was 59·11 days.

4. Toxicity was comparatively low in our series. 40% complained of vertigo. Eye and ear symptoms appeared when more than 60 gms. were given. No permanent injury was caused to any patient.

5. 72 out of 100 cases had far advanced lung tuberculosis involving both sides. 76% of cases improved considerably with treatment.

6. Best results were obtained in 26 cases with abdominal and laryngeal symptoms. 92·3% of these showed good results.

7. Streptomycin is a valuable adjunct to thoracoplasty. It was specially valuable for checking fresh contralateral spread and curing tracheobronchial symptoms which developed in these cases.

8. Empyema was not affected. Streptomycin reduced reduced the fever and improved the general condition and made the patients fit for thoracoplasty.

9. Symptomatic relief was the most remarkable feature. The fever was reduced in 75%, and the cough decreased in 66·6%. Improvement started from the very beginning of treatment.

10. Positive sputum was converted into negative in 55%. Eosinophilia developed in 48·9%.

11. X-ray improvement occurred in 60%. The most noticeable feature was the absorption of exudative infiltration more or less. In 32% cavities were reduced in size.

12. Contact dermatitis was noticed in one of the staff nurses who handled streptomycin. As a precautionary measure those handling streptomycin should wear gloves.

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A NEW ANTI-BACTERIAL AGENT DERIVED FROM THE DECOMPOSITION PRODUCT OF CRATAEVA ROXBURGHII

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Crataeva Roxburghii, Syn. *Barun*, is a tree of moderate size, with thick, grey bark, a much branched crown, and foliage thickly clustered at the ends of the twigs. The leaves are divided into three narrow pointed leaflets (Benthall, 1946). Various forms of this plant are wild in most parts of the plains of India, but not in lower Bengal, though it is abundant in some parts of East Bengal. Regarding the medicinal uses of the plant the above author mentions that the bark is considered good for indigestion and for promoting the appetite. The leaves are used to treat rheumatism and gout. The bark is also considered to be an important remedy in the Ayurvedic Pharmacopoeia for "calculus affections". From the decomposed bark of this plant a faintly cream-coloured, light crystalline substance has been isolated by J. S. Chatterjee and this substance forms the subject matter of the present paper. Chatterjee has found its melting point to be 144°C-145°C with empirical formula $C_{15}H_{16}N_2S$. On hydrolysis it yields two primary amines. It is insoluble in water, but soluble in ether. The substance could not be isolated directly from fresh bark, so it appears to be a decomposition product. It has been found that the same substance (same melting point, and the same physical and chemical characteristics so far observed) may also be isolated in the same way from several other plants (*e.g.*, Moringa Pterygosperma, Beng. Syn. *Sajina*, and, horse radish, Beng. Syn. *Mula*) where also it appears to be a product of decomposition.

Chopra *et al* (1932) isolated from Moringa pterygosperma, an amorphous base belonging to the sympathomimetic group and it closely resembled adrenaline and ephedrine in its effects, though much weaker. The substances isolated by Chopra have different physical and chemical characteristics.

Antibacterial Action

It has a strong antibacterial action, probably bacteriostatic in nature against cholera vibrio. Even when ½ mg. of this compound is suspended in 10 c.c. of the alkali-peptone solution and the media (drug 1 in 20,000) is then inoculated with cholera vibrio, it does not show any evidence of growth of the bacteria in 24 hours' time. Details of the action of this compound on the cholera vibrio and several other organisms are being studied and will be published in another paper.

Toxicity

When given by mouth toxicity of this compound seems to be low in guineapigs. Even 100 mg. of the

compound given orally, per kilogram body weight does not seem to affect a guineapig in any way. But cats succumb with 45 mg. per kilogram body weight orally in 22 hours. Human beings appear to be more susceptible. In some persons, even 4 mg. orally in a single dose, has produced unpleasant symptoms, *e.g.*, a sense of heat with flushing of the face and thirst and also an aching pain in the limbs which may last for 24 hours. But when given in divided doses, *e.g.*, 1 mg. every 6 or 8 hours it has produced no unpleasant symptom in any of the 60 persons in whom it has been used.

Clinical Trial in Cholera

The drug was given orally to 30 bacteriologically positive cholera cases admitted into the Chittaranjan Hospital during the period beginning from the first week of June to first week of August 1948.

Dosage of the drug—The drug was mixed with sugar of milk, and 1 mg. per dose was given orally to an adult every 6 or 8 hours till the symptoms subsided or the patient expired. Children aged 7 to 12 years were given ½ mg. per dose. Average total daily dose in most of the adult cases did not exceed 3 mg., and the drug was stopped as soon as the symptoms abated.

Other treatments—Besides this drug orally, intravenous saline transfusions (hypertonic, isotonic and alkaline) were necessary in most of the cases. 100 c.c. to 200 c.c. of 25 per cent solution of glucose were given intravenously to adults in 24 hours as a routine. Children received proportionately smaller doses. Atropine sulphate gr. 1/100 subcutaneously repeated after 8 to 12 hours, if necessary, was also given to adults, children receiving proportionately smaller doses. Other analeptics, *e.g.*, Coramine etc., were used according to necessity. Theophylline intravenously helped urination in some cases.

Examination of Stools

Collection of stools—On admission of the patient, and before commencing the drug, the stool was collected directly from the rectum by inserting a sterile rubber catheter per rectum. A part of this stool was used to inoculate the alkali-peptone media directly on the bed-side, while another part was examined microscopically.

Result of examination of stools—Out of the 34 cases studied in this series stools of 30 cases showed on microscopic examination characteristically motile curved bacilli, and on culture a positive growth of cholera vibrio was obtained. While in the remaining four, the stools on microscopic examinations alone showed motile curved bacilli but culturally they were negative. On microscopic examinations, besides curved bacilli, 23 specimens contained spirochaeta faecalis. Several others contained Entamoeba histolytica in vegetative forms, and in some cases various kinds of ova and cysts were found.

Description of Patients

Age—Of the 34 patients in this series, 3 were aged 50 years, 4 between 7 and 12 years, and the rest above 12 years and below 50 years.

Condition on admission—30 of these patients were admitted in a completely collapsed condition with no perceptible radial pulse in the wrist. The remaining 4 were admitted with feeble pulse. Vomiting, characteristic purging, dehydration, and anuria of some hours' duration were present in all the cases. One was pregnant for 7 months.

Results of Treatment

Death—6 patients died (aged 20, 45, 35, 39, 40 and 50 years respectively). The pregnant case had miscarriage, but recovered. Percentage of death—17·5.

Though the percentage of deaths in this series was lower than the average percentage of deaths amongst other cases of similar severity in the ward, one is to take into consideration the fact that the cases in this series were more or less specially selected for this particular investigation.

Vomiting—Effect of the drug on vomiting was marked. In 25 cases of this series vomiting was completely stopped after the first dose of the drug. In the remaining 9 cases too it was appreciably diminished.

Purging—Effect on purging was not appreciable during the first 24 hours. But it was checked or appreciably diminished during the next 24 hours.

Urine—As is to be expected in cholera cases the drug had no effect on the secretion of urine. Urinary secretion started with corresponding recovery of circulatory and kidney functions. Yet, out of the six fatal cases 4 started urinary secretion, before death, but they did not completely recover from the initial circulatory failure, and ultimately succumbed. Examination of the urine did not reveal any special abnormality due to the drug.

Saline transfusion—In this series, intravenous saline transfusions were given to 29 cases. In 5 other cases fluid was supplied orally, and all of them recovered. Two of the latter were admitted with imperceptible radial pulse, while three others had perceptible radial pulse on admission. Of these 5 cases, stool of one (with imperceptible radial pulse on admission) was only miscroscopically positive. Four others were culturally positive.

Effect on the cholera vibrio in the stool—This was studied in 23 cases. Stool was cultured every 24 hours till there was no growth of cholera vibrio. In 22 cases (95·65 per cent) stool became culturally negative in 72 hours; in 15 cases (65·2 per cent) in 48 hours, in 3 cases (13·04 per cent) in 24 hours, and in 1 case (4·35 per cent) in 5 days. In the last case the patient (aged 7 years) received the total quantity of 1½ mg. of the drug only. Further administration was stopped as the symptoms subsided and also for further observation as indicated later. The total quantity of the drug administered

before the stool became culturally negative is shown in Table I.

TABLE I—SHOWING THE TOTAL QUANTITY OF THE DRUG ADMINISTERED

Total quantity in mgm. of the drug administered before the stool became culturally negative.	*Total number of cases in whom stool became bacteriologically negative with that quantity of the drug.*
1	3 cases
2	4 cases
3	2 cases
4	5 cases
5	3 cases
6	2 cases
7	2 cases
9	1 case

(*a*) Total quantity of the drug administered in those cases in whom stool became culturally negative in 24 hours was,

Minimum—2 mgm. Maximum—4 mgm.

Average per case (total 3 cases only) 2·7 *i.e.* 3 mg.

(*b*) Total quantity of the drug administered in those cases in whom stool was culturally positive after 24 hours but became culturally negative in 48 hours was,

Minimum—1 mgm. Maximum—9 mgm.

Average per case (total 15 cases only)—4 mgm.

(*c*) Total quantity of the drug administered in those cases in whom stool was culturally positive after 48 hours but became culturally negative in 72 hours was,

Minimum—4 mgm. Maximum—6 mgm.

Average per case (total 4 cases only)—4·75 mgm = 5 mgm.

(*d*) Total quantity of the drug administered in the case in whom stool became culturally negative in 5 days (1 case only, aged 7 years)—1½ mgm.

Total quantity of the drug on an average administered to each of the cured cases during the course of treatment (including 4 cases aged 12 years or below receiving ½ mgm. per dose) is shown below:

Minimum.	*Maximum.*	*Average per case* (total 28 cases only)
1 mgm.	10 mgm.	4 mgm.

Total quantity of the drug on an average administered to each of the fatal cases during the course of treatment—

Minimum.	*Maximum.*	*Average per case* (total 6 cases only)
2 mgm.	4 mgm.	3·3 mgm.

DISCUSSIONS

This compound appears to have a strong antibacterial action possibly bacteriostatic in nature in the dosage used against cholera vibrio both in human beings and *in vitro*.

Stools from cholera cases became culturally negative (of cholera vibrio) with very minute doses of this compound, and in a very short time—within 72 hours in more than 95 per cent of the cases examined, within 48 hours in more than 65 per cent, and in 24 hours in a little above 13 per cent of the cases.

Toxicity of the compound is very low in guinea-pigs, when administered orally—100 milligrams per kilogram of body weight producing no change in the normal condition. But in human beings, in some persons, disagreeable symptoms have been produced with such minute dosage as 4 mg. in a single dose.

This compound, on hydrolysis has been found to yield two molecules of primary amines. Barger and Dale (1910) have found that sympathomimetic action is possessed by a large series of amines, the simplest being primary fatty amines. All the substances producing this action in a characteristic manner were found by them to be primary and secondary amines. Vomiting was quickly controlled in most of the cholera cases in this series after commencement of the drug, and this occurred long before the stool became bacteriologically negative, possibly due to sympathomimetic action of the amine component of the drug. Symptoms of cholera indicate a violent disturbance of the balance of the autonomic nervous system. In the compound under review, there is probably a combination of the bacteriostatic action with sympathomimetic action, and as such, the drug is likely to prove useful in this disease. In five comparatively mild cases in this series no saline transfusions were given, yet the patients made uneventful recovery. From the fact recorded above further clinical investigations with the drug especially in the early stages of cholera, appear advisable.

The drug, even in minute dose (1 to 2 mg.) appears to produce a slow but sustained action on the cholera vibrio in the human stool. To study this aspect the drug was administeed in 8 cases during the first 24 hours only and then stopped, stools being cultured every 24 hours. Total dosages given in 24 hours were, 1½ mg., 1 mg., 1 mg., 2 mg., 2 mg., 1 mg., 2 mg., 2 mg., respectively. In 2 cases the stool became culturally negative (of cholera vibrio) in 24 hours. In five others the stools showed the presence of cholera vibrio after 24 hours, but became free of it in 48 hours. Only in one case it took 5 days for the stool to become negative on culture. This characteristic of the drug may be useful for prophylactic use in contacts, if on further experience the drug is found to be sufficiently safe for mass use. Incidentally it may be mentioned that this drug has been found to

be effective in several cases of acute diarrhoeas, and also in cases of colitis with symptoms of dysentery.

Summary

1. A new antibacterial compound derived from the decomposition product of Crataeva Roxburghii (Bengali Syn. *Barun*) bark has been tried in 34 bacteriologically positive cholera cases.

2. It has been found to have a strong antibacterial action, possibly bacteriostatic in nature in the dosage used, against cholera vibrio both *in vitro* and in human cholera stools.

3. Toxicity of the drug in guinea-pigs, when administered orally, is very low. 100 mg. per kilo. body weight did not produce any effect. But in some human adults even 4 mg. orally in a single dose produced unpleasant symptoms, *e.g.* a sense of heat with flushing of the face and thirst, and also an aching pain in the limbs, which lasted for 24 hours.

4. Dosage used in this series has been one mg. every 6 or 8 hours orally till the symptoms subsided. Average total daily dose in most of the adult cases did not exceed 3 mg.

5. Vomiting has been quickly stopped in most of the cases on the commencement of the drug, and this action was produced long before the stools became bacteriologically negative, possibly due to sympathomimetic action of the amine component of the drug.

6. Cholera vibrio disappeared from the stools within 72 hours in more than 95 per cent of the cases. Total quantity of the drug taken before the stool became culturally negative varied from 1 mg. to 9 mg. in different cases.

7. The drug, even in minute doses (1 to 2 mg) appears to have a slow but sustained antibacterial action on the cholera vibrio in the human stool, and as such its use as a prophylactic in contacts is suggested, if on further experience the drug is found to be sufficiently safe for mass use.

Acknowledgment

My best thanks are due to Mr. J. S. Chatterjee for not only preparing but measuring out the minute quantities of the drug in chemical balance, for the study in this series, to Dr. S. K. Dutta of the Pathology department of the Calcutta National Medical Institute for carrying out all the microscopic and bacteriological examinations, to my house physicians Drs. Ranjit Sanyal and Barun Chowdhury and their associates, and also to the nursing staff, but for whose active co-operation it would have been impossible to carry out this investigation.

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A STUDY OF CLINICAL FEATURES OF ACUTE CARDIAC FAILURE IN EPIDEMIC DROPSY

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Introduction

At Bhagalpur, epidemic dropsy is reported to have had a flare in the years of 1939-40. Since then sporadic cases have been reported off and on in the following years. From the months of January and February, 1947, dropsy seemed to be taking the epidemic form again, and the curve went on rising till it reached the highest level during the months of April and June. The apex of the curve formed during these three months was rather flat. Then there was a strong agitation against contamination of mustard oil following which the curve showed a gradual decline in the months of July and August after which only sporadic and residual cases were met with.

That the attack of epidemic dropsy was due to contaminated mustard oil is borne out by the following facts:—

(1) The disease occurred in all grades of economic or social class.

(2) No case was found in the local Marwari community which does not use mustard oil in its food.

(3) At Sabour, in the colony of the staff of the College, the disease was found prevalent amongst the Bengali and Behari communities, but not in those who came from northern and western India and who did not take mustard oil in their food.

(4) Mustard oil obtained from the market was used in the food of all the affected families.

(5) The samples of mustard oil obtained from the affected houses invariably gave positive reaction with the nitric acid test.

(6) After the institution of measures against the contamination of mustard oil, the epidemic seemed to subside.

(7) In most of the cases, a histroy of a number of their family members being simultaneously affected was obtained.

Material for Study

The records of only 50 cases could be obtained by the writer which included:—(*a*) Hospital cases: (*i*) indoor—9, (*ii*) outdoor—33; (*b*) Private cases of acute cardiac failure—8.

The cases can be divided into two broad clinical groups *e.g.*:—

(I) Simple and associated with or without other organic diseases, like kalazar, dysentery and hepatitis—this group numbered 38.

No other special clinical features, except the usual, marked the first group. The signs of the lesions of the skin and eyes were not present in them, and in

only very few cases gastro-intestinal symptoms were the presenting or the marked features of the cases.

(II) Cases which had attacks of acute cardiac failure—12 cases.

The presenting symptom of these cases was marked orthopnoea, more or less persistent, and unresponsive to all the routine treatments of cardiac failure.

The following points distinguished this group from the other organic diseases of the heart:—

(1) No organic valvular lesions were detected.

(2) No previous history of rheumatism, syphilis, or symptoms of cardiac failure was obtained though they appeared as fairly advanced cardiac cases.

(3) No ascites was present.

(4) No enlargement of the liver was detected.

(5) Cyanosis was not present in most of them except in a few just before death.

The points which indicate their causative factor as epidemic dropsy are as follows:—

(1) Several cases cropped up between the end of April and June and there has been definite subsidence in the incidence of such cases from July onwards. This periodicity corresponded with that of epidemic dropsy.

(2) In 7 out of the 12 cases definite history of symptoms of epidemic dropsy in several members of the family was available.

(3) All the 12 cases were taking mustard oil obtained from local sources in their food for sometime before they developed these acute symptoms.

(4) The mustard oil obtained from 7 of the families gave positive results with the nitric acid test. It was not positive in the sample received from the fourth family of the series.

(5) Among the 12 cases, 8 belonged to the middle and 4 to the lower middle class.

That the above cases with severe dyspnoea were not cases of primary lung disease was shown by the facts that:—

(1) They had no previous history of asthma.

(2) The dypnoea after its onset was progressive in most of them.

(3) They did not respond to broncho-dilator drugs.

(4) Fever and toxaemia were not the dominant signs with them.

Clinical Picture

The onset was acute. They were highly dyspnoeic. The respiration was hurried and the respiration rate usually went upto 50 to 60 per minute. The pulse usually was very rapid and commonly went upto between 120 and 130 per minute. The temperature at the same time did not show any significant rise and was usually below 99°F. Usually the patient preferred sitting on bed to lying down. Nevertheless they remained dyspnoeic in every posture that could be adopted. Sitting forward with pillows under their abdomen was the posture which some of them preferred. Rales and rhonchi were audible all over the lung areas. The first sound of the heart was usually weaker than normal and often equal in intensity to the second sound both in mitral and pulmonary areas. The character of the first sound was either muffled and prolonged or short and sharp. In the latter case the sounds had a tic-tac rhythm. The apical impulse was feeble and at times diffuse over more than one intercostal space. Dilatation of the heart on the left side was observed in some of the cases. Slight oedema of the feet and the legs was noticed in some of the cases. It was interesting to note that dropsy was not a very marked feature in these cases specially as noticed at the time of examination. Only in 3 of the cases slight pitting of the feet and legs on pressure was observed. In some of them, history of oedema of the lower extremities for sometime antecedent to the cardiac attack was obtained. The blood pressure, both systolic and diastolic, was either subnormal or normal.

Among the 12 cases, two of them had attacks lasting for short periods varying between 2 and 4 hours. One of them had protracted attack lasting for 48 hours. In the remaining 9 cases, dyspnoea continued, gradually increasing in severity, unresponsive to treatment and finally terminated in death.

Discussion

These probable cases of epidemic dropsy were important in view of the facts that (1) The cardiac attacks were unexpected and sudden, and (2) lack of their response to treatment and consequently the high death rate among them.

In some of the cases, where the cardiac symptoms were observed personally by the writer (3 cases) they resembled cardiac asthma. The attacks were rather persistent and malignant due to apparently marked invalidity of the myocardium. It may be mentioned here that cardiac asthma has some special features differentiating it from dyspnoea which gradually sets in with decompensation in cardiac affections. In the latter group, the onset is gradual and generally evidences of right sided heart-failure, cyanosis, oedema of the lower extremities, ascites and enlargement of liver are present. The anoxia in this condition is attributable to morbid changes both at the peripheral

i.e. at the tissues and central *i.e.* cardio-pulmonary. At times, cases of marked left sided failure are met with, where the cardiac output being markedly lowered, dyspnoea with anaemic anoxia sets in. On the other hand in cardiac asthma, the dyspnoea is chiefly due to acute left ventricular failure resulting in acute pulmonary oedema and blockade. Markedly inefficient myocardium suddenly failing in its work is at the root of this condition.

There is usually disproportionate activity between the two sides of the heart, the right side working well while the left side falls back. Cardiac asthma has been described in medicine as paroxysmal dyspnoea occurring in conditions like hypertension, aortic incompetence, chronic myocardial disease, ventricular heart-block, diseases of the coronary arteries, and infrequently in mitral stenosis with increased pulse-rate. Herein the condition may be placed in close proximity with the chronic myocardial disease with the qualification that the paroxysm is rather more acute and lasting and most often terminating in death within a short period.

How do these cases differ from others of Epidemic Dropsy?

Is it possible that in certain cases, the argemone toxin has greater predilection for the heart than the peripheral arterio-capillary beds?

Is it possible that the muscles of the myocardium in these cases are affected besides the blood-vessels of the heart?

Is it a fact that in these cases the onset of the disease is slow with less manifest symptoms, the disease continues for sometime, the patient pursues his usual activities largely negligent of the developing changes in him with occasional palpitation and dyspnoea on exertion taking a few injections now and then for his satisfaction but still not taking requisite rest so that the myocardium is progressively damaged due to lack of rest and protracted poisoning till a sudden and unexpected attack of cardiac failure supervenes?*

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The writer is thankful to Dr. P. Gupta, Civil Surgeon, Bhagalpur, who has not only provided him with valuable data from his personal observation but has also encouraged and directed him to write this article.

(NOTE.—No case of Epidemic Dropsy has been reported during the corresponding months of 1948. Obviously this is due to the agitation and measures taken against the contamination of mustard oil in 1947).

* If the author refers to the pathological work done by De, De and Chatterjee and De and Trivedi he will find the cause of sudden failure clearly explained.—EDITOR, *J. Indian M. A.*

SPECIAL ARTICLE

RECENT TRENDS IN PATHOLOGY TEACHING AND HOSPITAL SERVICE

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(Continued from previous issue)

It has been said that the standard of the pathology department in any hospital is an accurate measure of the standard of the hospital as a whole. The department is called upon to render the following services to the hospital:—

1. Maintenance of an adequate laboratory of surgical pathology to examine and diagnose tissues removed at operations.

2. Maintenance of a diagnostic bacteriological, serological, chemical and clinical pathology laboratory.

3. Performance of post mortems with a view to determine the nature of disease and cause of death, besides helping the clinicians to gauge the results of treatment.

I strongly maintain that rendering an adequate and prompt hospital service is as essential for the integrity and reputation of a good department as the nature of research and original work published. Pathologists in their zeal for teaching and research may tend to neglect the routine diagnostic work, which ultimately results in dissatisfaction among the clinical staff, who in turn demand separate diagnostic laboratories. This is what has happened in many medical colleges of the United States, where the pathology departments are responsible only for teaching pathology and performing the autopsies. The clinical departments have their own diagnostic laboratories, which are well equipped and staffed. However no one is satisfied with this arrangement, because not only does it mean unnecessary expenditure, but the department of pathology is starved for the material which is so essential for teaching and research. Efforts are being made to merge all the laboratories into the present department.

The usefulness of the pathologist to the hospital does not, however, finish with the 'prompt service' to the clinicians. He is a member of the hospital team and as such should be regarded as a consultant. It is therefore essential for the pathologist to see the patients in the ward and to encourage the clinicians

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to come to the laboratory to see slides from their patients and autopsies. Similarly the pathologist should be given research beds in the wards, as also the clinician, laboratory facilities to carry on his research projects.

Surgical Pathology Laboratory

Examination and diagnosis of tissues removed at opertion should be prompt, and not more than 72 hours should lapse between receiving the tissues and sending the diagnosis. I find that an autotechnicon is a definite asset to the department. If properly used diagnosis on tissues can be given within 24 hours with its help. All tissues removed should be carefully examined and detailed gross description given. It is always useful to save tissue until the final diagnosis has been given, in case the important lesion is missed at the first cut. Sample tissues should be saved on all surgical cases indefinitely.

Not infrequently the diagnostic aid of the pathology department is sought by the surgeon during the operation to decide the nature and extent of treatment. An immediate microscopic examination is carried out on a frozen section and a report given to the surgeon before the operation is completed so that he may modify his operation in the light of the pathological diagnosis. For this purpose it is necessary to have a small laboratory furnished with a freezing microtome and a microscope. The pathologist should be available in the department to go to the operating room to examine the frozen section. An alternative would be to send the tissue to the department. Adoption of one or the other method will depend upon facilities of communication available between the laboratory and operating theatre.

A complete record should be kept of surgical tissue, including a brief clinical history, gross description of the tissue and the microscopic findings, with the paraffin blocks and the sections. Similarly each autopsy performed should have a complete protocol, the microscopic sections, paraffin blocks and the pieces of organs. All the slides should be cross indexed under lesion, organ, and patient's name, besides a card for each case giving a brief clinical history, gross and microscopical findings. A well indexed slide file is, as Shields Warren says "the heart of the laboratory." It is this collection which forms the basis of special research, which of course may have to be augmented by experimental work.

Clinical and Bacteriological Laboratories

To be of any help to the clinicians the examinations should be carried out as promptly as possible, and a twenty four hour service should be available. At the Agra Medical College the routine examinations for the patients admitted to the hospital are carried out in the central clinical laboratory and the individual ward laboratories of the Thomason and allied hospitals. In the former the work is done by the resident pathologist, and in ward laboratories by the house officers. The central laboratory is well equipped to perform the routine pathological and bacteriological examinations including emergency cultures. All the complicated tests are done in the department. The tests for the outpatients are done in the pathology laboratory of the outpatient department, which is staffed by another resident pathologist. The residents are on night call in the hospital on alternate days and are provided with accommodation in the hospital compound.

Postmortem Service

The performance of systematic autopsies is the most important duty of a department of pathology. As Karsner[2] has pointed out, the autopsy includes more than mere, "dissection of the dead body for the purpose of ascertaining the cause, seat, or nature of a disease." We have to consider its signficance from the point of view of its value to students, doctors, relatives of the deceased and the state.

Farber[12] discussing the significance of autopsy in teaching the medical student writes, "he should be encouraged to develop the autopsy habit early in his career. The cultivation of the habit throughout his future practice of medicine should furnish him a source of information that will yield an objective evaluation of the accuracy of clinical diagnosis, and efficacy of treatment." One of the outstanding merits of the present medical curriculum is the opportunity afforded to the student to observe a patient in the wards and in the operation room, and if death should occur, in the post-mortem room.

The clinician looks to the autopsy for an answer to many unexplained episodes during life, and for an accurate cause of death.

To the pathologist it gives the wealth of information regarding the morbid anatomy of the diseased process, and valuable material for research. The present progress of clinical medicine is largely due to perfection of autopsy technic. As Farber[13] writes, "Before adoption of the complete autopsy, clinical medicine rested upon scattered observations of great merit, obscured in considerable part by the hopeless speculation concerning the seat, cause and nature of the disease. The autopsy substituted the dead house for the savant's arm chair, as a source of information about disease. By its means, objectivity of thought and method replaced the more comfortable but disastrous practice of building complex classifications of disease from the fertile brain of the non-observing thinker." *Mortui vivos docent* (The dead teach the living)—the motto on the walls of the autopsy room in Shields Warren's laboratory summarises the significance of the autopsy. Morgues are to be regarded and maintained as the operating rooms of the pathology department, and the autopsies are to performed with the skill and care of a major operation.

It was not until I had worked in the laboratories of Shields Warren, Sydney Farber and Howard Karsner, that I realised that—

The significance of the postmortem to the surviving relatives is twofold. To quote Farber[13] again, "as members of society, they should assist in the accumulation of knowledge which may result in prevention or earlier recognition of disease in other human beings. Such a contribution to the knowledge of the world and to the welfare of mankind is a form of philanthropy not fully appreciated, yet possible for people of any status. Of more immediate interest to the relatives is the fact that the autopsy yields a more complete explanation than is otherwise possible, of the development of the fatal disease and the cause of death. This may have a direct bearing on the health of the other members of the family."

To the state it affords the only reliable source of information on the causes of death. In our country with the present paucity of autopsies, such vital statistics are collected on the basis of clinical diagnosis, and these are frequently inaccurate. This has been largely responsible for our failure to control epidemics in India, since with no autopsies sporadic cases of infectious diseases are often missed.

To perform an autopsy in India, the written permission of the nearest relative must be secured, but as a rule this is refused. Only unclaimed bodies have been available for post mortem study, and lately even these have been difficult to obtain due to the formation of religious bodies like Samaj and Anjuman, which have assumed the responsibility of disposing of the dead. I can do no better to impress upon the public and the doctor, their right path of duty than to quote what Donatus[14] wrote in 1586: "Let those who interdict the opening of bodies well understand their errors. When the cause of a disease is obscure, in opposing the dissection of a corpse which must soon become the food of worms, they do no good to the inanimate mass and they cause a grave damage to the rest of mankind; for they prevent the physicians from acquiring knowledge which may afford the means of a great relief eventually to individuals attacked by similar disease. No less blame is applicable to those physicians who, from laziness or repugnance, love better to remain in the darkness of ignorance than to scrutinize laboriously the truth, not reflecting that by such conduct they render themselves culpable towards God, themselves and society at large."

Due to the efforts of Virchow, Rokitansky and recently Lubarsch, the highest percentage of autopsies was found in Germany and Austria, where a liberal interpretation of the law sanctioned performance of autopsy on those dying in the hospitals. In America most of the teaching hospitals claim an average of 50 to 60 per cent autopsies. The American Medical Association only requires fifteen per cent for class A hospitals. Yet if the country as a whole is considered, Karsner[2] has estimated that the autopsies in America are performed on less than seven-tenths per cent of dead, while Lubarsch[15] for Germany computed a rate of five per cent. The figures for India are not available, but I know, would compare unfavourably.

The number of autopsies performed varies directly with the interest of the clinician and the efforts they and their house-officers exert to secure the permission. In America students are advised to select hospitals for internships on the basis of autopsies performed and autopsy percentage is the best single criterion of the teaching effectiveness of a hospital (Christian[16]).

In India as elsewhere, the permission for postmortem study is refused on sentimental or religious grounds. Both Hindus and Muslims assert that religion prohibits performance of postmortem, although as far as I know, none of the religious books state anything prohibitory to autopsy. However the objections based on sentiment are the most difficult to overcome and only the attending physician is in a position to overcome them. His success will depend upon how far he has convinced the relatives of his efforts to save the life of the patient, and the amount of human sympathy he has shown. He should ask the permission as a reward of his labours. but he must be autopsy-minded before he can be do so (Mills[17], Hoffman[18] and Hammond[19]). It is difficult to get permission from the religious bodies like Samaj and Anjuman, and the only solution in these cases is to seek Government legislation requiring all unclaimed bodies to be autopsied before being handed over to the respective organisations for disposal.

No autopsy service is complete without a system of maintaining autopsy protocols. These should be as complete as possible, and should contain clinical history, gross and microscopical findings, and bacteriological and chemical studies. A summary with clinico-pathological correlation may be appended at the end. Photographs of the gross findings should be attached, while well-indexed microscopic slides should be kept. It is advised to follow a definite line of protocol writing, as well as having a standard form for taking dictation notes. This material will always be consulted by clinicians, pathologists and medical students, and will many times form the basis for further research.

Finally, I would impress upon the pathologists and clinicians, the necessity of meeting regularly on a common platform. The clinician with a proper conception of the work of the laboratory, its limitations, and sources of error, must be matched by the pathologist with an understanding of the difficulties which attend the diagnosis and treatment of disease in the living patient. For this purpose it is necessary to have medico and surgico-pathological conferences, where besides the autopsies, any other subject may be discussed. Let the clinician and the pathologist regard

(Concluded at foot of page 164)

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TEACHING OF PATHOLOGY

That the present method of medical education is not producing the ideal doctor, has been recognised by all thinkers in our profession. And sub-committees have been formed by all medical bodies to come to a conclusion regarding the future programme. To this end we also printed quite a number of articles on the subject. One such article which is being concluded in this issue is by Wahi on "Recent Trends in Pathology Teaching and Hospital Practice". In it he has described the methods of teaching pathology in the U.S.A.

Pathology is an important subject and as such requires detailed consideration. At the present moment, too much time is being spent on unnecessary details and fundamentals are often lost sight of. An example of what might be an ideal procedure can be found in the article by Wahi[1] but certain other points on the subject may also be discussed.

British Medical Association has recently published a brochure on medical education.[2] This Association has dealt with some amount of thoroughness all the subjects included in medical curriculum. The report rightly points out that the value of pathology and bacteriology to a medical man is to make him appreciate the etiological factors involved in the diseased man and to understand the basis of the symptoms for which the patient comes. To the medical man the knowledge of preventive medicine, medicine of the future, also depends on the adequate knowledge of pathology and bacteriology. We agree with Wahi[3] when he writes, "our primary aim in teaching medical students should not be to produce expert pathologists, but rather good general practitioners equipped to visualise the underlying pathological changes and to fully appreciate the clinical course of the disease." Hence it is unfortunate that pathology has so long been divorced from clinical medicine. One may note that in ancient India, the makers of Ayurveda preferred to combine pathology and clinical medicine under the common term 'Nidana'.

"The principles of pathology, taught without demonstration in the living subject, are likely to seem abstruse and unreal to the student, and has at present too little opportunity of correlating his knowledge of pathology with what he learns in the wards."[4]

So the teaching of pathology will naturally be done in the period when the student is learning clinical methods. Here the pathologist and the clinician must co-operate. The student should understand that pathology and clinical medicine go hand in hand. They are just two parts of one whole subject. If this is the aim of teaching pathology, then a few corollaries naturally follow. That bacteriology, immunology, hæmatology, serology and pathology form one subject. There is no sense in teaching them separately. If this overall picture of pathology is kept in mind, no part will ever grow at the expense of the other. Each part will fall in the right place. Useless mass of details, as necessary for the specialist, shall have to be eschewed, and the whole curriculum kept to the broad basic facts. To-day the medical graduate is obliged to learn a mass of facts which hides the basic principles. Regarding techniques, is it necessary that a doctor should learn the bacteriological, biochemical, histological techniques as given in modern text books? If we accept the teaching principles as enunciated above, the answer is definitely 'No' because none of these are basic knowledge so far as clinical medicine is concerned. The same applies to special pathology. A *detailed study* of special pathology is again useless to the ordinary doctor.

Then again the *proper place of laboratory* in medical diagnosis should be stressed. Laboratory methods, technique and appliances are growing by leaps and bounds. It is not possible and not necessary for the general practitioners to keep abreast with the details of the complicated technique and possess the ever-increasing appliances for the laboratory test, hence has grown a speciality of laboratory workers. Although the speciality is undoubtedly necessary and helps the clinician to an admirable extent still it has got its drawback. The modern clinician has the trend to depend on this speciality too much and a patient may be required to bring a bundle of labora-

[1] WAHI, P. N.—*J. Indian M. A.*, **18**:101, 1949.
[2] The Training of a doctor—Butterworth & Co. (Publishers), Ltd., London.
[3] WAHI, P. N.—*J. Indian M. A.*, **18**:101, 1949.
[4] The Training of a Doctor—Butterworth & Co. (Publishers), Ltd., London, p. 72.

tory reports, skiagrams and electrocardiograms etc. and the clinicians may not require to examine the patient clinically. When these clinicians become teachers of medical institutions, the students in their turn imbibe this teaching and that is very often reflected in their filling up of the history-sheets of the patients in their charge. In teaching institutions one may often find the case-sheets blank and the teacher taking no note of that. When these students become general practitioners in big towns providing proper laboratory facilities, they can manage according to the purse of the patient to secure the expensive laboratory reports but their colleagues in the rural areas find themselves in deep water. That laboratories also can tell lies should be demonstrated. On the other hand all medical graduates must know how to do simple clinical examinations *e.g.* total and differential count of blood, identification of malarial parasites or L.D. bodies, routine urine and stool examination. In order to get the full benefit of the laboratory findings, they must possess a thorough knowledge of how to collect the proper material for laboratory examination and send them to a distant laboratory, by post if required. This can be ensured by some such procedure as "In the final year a clerkship in pathology for a month." This "will serve to consolidate students' knowledge and its application."[5] This clerkship shall have to be done in the medical department.

General Medical Council recommended that each student should act as a post-mortem clerk in at least ten cases. If sufficient autopsies can be arranged this practice will surely ensure integration of pathology with the clinical symptoms.

With the new medical curriculum in the making we recommend these suggestions to the personnel sitting to formulate the details.

[5] Training of a Doctor (*loc. cit.*).

(*Continued from page 162*)

themselves indispensable to each other in their profession as well as in the pursuit of knowledge. Sympathy and harmony between the two are essential to the progress of medicine.

ACKNOWLEDGMENT

I am indebted to Dr. Sydney Farber, Pathologist to the Children's Hospital and associate professor of pathology, Harvard Medical School, and to Professor Charles E. Dunlap of the Tulane University of Louisiana School of Medicine, for going through the manuscript and offering valuable suggestions.

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I wish to gratefully acknowledge the constant help that I received from Miss Gretchen R. Riese of the Harvard Medical School library in the preparation of this manuscript.

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NOTES AND NEWS

X-RAY PLANT FOR JORHAT SANATORIUM

Sri Padmanath Sarma of Chenijan, Jorhat, Assam, has made a gift of one D-3-38 X-ray apparatus costing over Rs. 30,000 to the Tuberculosis Sanatorium at Jorhat. The Sanatorium, the only one in the province of Assam for treating tuberculosis cases, has been opened recently.

STATE MEDICAL FACULTY OF WEST BENGAL

Sri M. N. Gupta, the Secretary writes:—

It is hereby notified for the guidance of all concerned that the title granted under articles 6-A and 6-B of the Statutes of this Faculty, is "L.M.S. (Nat)", and not "L.M.S.", and it cannot be altered by the omission of any portion of it such as "Nat."

WEST BENGAL COUNCIL OF MEDICAL REGISTRATION

The following abstract of important items of the minutes of the Council at a recent meeting are published for general information:

1. The following resolution which was passed by the Madras Medical Council at their meeting in March 1948, was adopted:

"That the primary registration of basic qualification should be in the register of the Council in whose jurisdiction the University or Examining Body is situated."

2. The Council directed the removal of the name of a practitioner from the Register under section 25 (*a*) of the Bengal Medical Act for having participated in the dispensing of a prescription which had 5 grains of quinine, by giving only 0·71 grains.

3. The Council directed the removal of the name of a practiotioner from the Register under section 25 (*a*) of the Bengal Medical Act for giving untrue and improper certificates.

4. Two practitioners had given misleading Yellow Fever inoculation certificates. The Council warned them and required them to submit in the first week of July, 1949, certificates from two registered practitioners of their professional conduct, the final order being kept pending till the meeting of the Council in August 1949.

5. The Council recommended to Government the recognition of the M.B.B.S. degree of the Agra University as a qualification registrable under the Bengal Medical Act, 1914 and the amendment of the Schedule to the Act accordingly.

BOMBAY MEDICAL BRAINS TRUST

K. K. Dadachanji, Jt. Hony. Secretary, Grant College Medical Society, 13, Jenkin's House, Mereweather Road, Bombay, writes: The Grant College Medical Society has resolved to inaugurate the Bombay Medical Brains' Trust for the benefit of all classes of the medical practitioners of Bombay—whether general, or consultants or specialists, to satisfy a long standing need for solving the many and varied problems facing the profession from day to day. There is no organisation in our city which can satisfy the need. The proposed Brains Trust will be open free to all practitioners of allopathic medicine irrespective of their membership of our Society, as one of the main objects of the Trust will be to disseminate correct and uptodate information on the whole group of the basic medical and ancillary and allied sciences as well as the Art and Practice of Medicine and Public Health and Research.

The panel of the Medical Brains Trust will consist of 5-7 medical experts, one of whom will serve as the question-master or chairman. The members of the panel will vary from meeting to meeting, which in the first place will be held on a fixed date in each month.

AUSTRALIAN NATIONAL HEALTH SCHEME

The Australian Federal Cabinet recently approved plans for a national health service to provide free almost every type of medical attention. The Minister for Health (Senator McKenna) will introduce legislation soon to set up an administrative unit for the scheme.

The scheme will not begin to operate until late next year. The Government will not announce details of the scheme until Caucus has discussed it and suggested any changes. Experts estimate the cost of the scheme when it is in full operation at between Rs. 16,00,00,000 and Rs. 21,40,00,000 a year.

The Government plans include:

Free diagnostic and treatment facilities for people up to any age.

Free dental treatment for children, probably up to 14 years of age.

The administrative unit will be either a corporation under ministerial control or a section of the Health Department.—*Australian Med. News Letter.*

MEDICAL SCHOOLS IN GERMANY

On the invitation of the American authorities, representatives of the General Medical Council, the Royal College of Physicians and the Royal College of Surgeons visited the American zone of Germany and interviewed both members of the United States Medical Service and German teachers and practitioners, in order to assist the Government of the

American zone by informing them and the Germans of the system of medical education in England, the discipline of the medical profession and the new National Health Service. They visited Frankfurt, Heidelberg, Stuttgart, Munich, Erlangen and Wurzburg and had discussions with the deans and professors of the medical faculties and also with representatives of general practitioners. A striking feature of the German situation was the immense number of persons who desire to take up a medical career. At Heidelberg there were 1,600 applicants for one hundred and fifty vacancies. At Munich there were 3,000 medical students. In spite of decisions for their reduction, the number itself forms a serious problem for the university. The difficulty is increased by the serious depletion of the teaching staffs, the destruction of hospital buildings and laboratories and the lack of funds. In order to obtain clinical experience many doctors have taken up posts as unpaid assistants at the hospitals. In Frankfurt, for example, Professor Volhard has 16 paid and 51 unpaid assistants in his large medical clinic. The unpaid assistants live a precarious life, subsisting on the charity of their relations or friends, often with insufficient food. The plight of the students is even worse, for housing accommodation is totally inadequate and books almost unobtainable.

The needs of the medical faculties are both financial and academic. More money is required for the rebuilding of hospitals and laboratories, for the payment of more assistants and especially for the payment of research students. At present little or no research is done because of lack of funds. The serious shortage of German textbooks is unavoidable, but the medical schools are also starved of foreign journals, which they cannot buy because of lack of dollars and sterling. This visit was to the American zone only, but it was ascertained that the same conditions prevail in all the medical schools of Germany. The representatives end with a plea for assistance to Germany "if only as an acknowledgement of what we owe to German medicine in the past."—*J.A.M.A.*, **138**:768, 1948.

THIRD CONGRESS OF SOVIET NEUROPATHOLOGISTS & PSYCHIATRISTS

Dr. B. Lilin, Moscow, writes:—The Third Congress of Neuropathologists and Psychiatrists of the Soviet Union which took place in Moscow was attended by some 2,000 delegates and guests from all ends of the country, including medical practitioners-specialists, and research workers from Soviet institutes of the brain, neuro-surgery, psychiatry. The different, constructive trends and schools of Soviet neurology and psychiatry, which have been formed in the past thirty years not only in the capitals but also in the provinces of the USSR (Rostov-on-Don, Molotov, Kharkov, and so on) were represented at the Congress.

The numerous papers delivered and the ensuring discussions clearly reflected the vast scope of research in the USSR, the close contact between Soviet neurology and psychiatry, on the one hand, and the achievements of Soviet physiology, the brilliant experimental researches and view-points of Russian scientist-materialists, such as Pavlov, Vvedensky, Semoilov, Ukhtomsky and so forth, on the other.

This contact is particularly understandable if we take into consideration that the materialist teachings of the great Russian physiologist, Ivan Pavlov, on the laws governing the higher nervous activity, proved to be the key to the understanding of many complicated diseases of the nervous system, that Pavlov's conception on sleep, on the relations between the cortex and the subcortical sphere helped us to understand a number of mechanisms of certain pathological processes of the brain. As we know, the principle of treating psychic and nervous disorders with sleep was born of Pavlov's ideas on the role of protective inhibition. On the basis of the teachings of eminent Soviet physiologists, pupils of Pavlov's school (L. Orbeli on the physiology of the vegetative nervous system, and K. Bykov on the relationship between the cerebral cortex and the internal organs), the psychosomatic tendency is being successfully developed in Soviet medicine.

It was, therefore, not accidental that L. Orbeli's general theoretical paper on the importance of the second signal system in the analysis of psychic functions attracted great attention at the Congress. The speaker noted that Pavlov, when studying conditioned reflexes, regarded all reflex effects as signal effects, enabling the animal or man to react to any given phenomena in the environment before these have had the opportunity to exercise any important influence on the organism.

To determine the physiological mechanisms on the basis of which the second signal system originates means to understand the significance of disturbances of this system, which frequently deprive man of the possibility of intercourse with his surroundings. It is also important to establish the relation of the second signal system to the first signal system, common to man and the great majority of animals. In the Soviet Union, physiologists, neurologists and psychiatrists are collaborating in the elaboration of these extremely complicated problems.

E. Sepp, member of the Academy of Medical Sciences of the USSR, in his report showed, by a number of examples, the immense role of clinical observations in studying the physiology of the nervous system. Professor P. Grashchenkov outlined the physiological trend in neurology, concentrating his attention chiefly on the teaching of synapsis. S. Sarkisov, member of the Academy of Medical Sciences of the USSR, devoted his report to problems of the localization of functions in the cerebral cortex in the light of certain data on interneuronal connections. The considerable successes achieved by Soviet scientists in elaborating these problems are the result both of excellently organised clinical and experimental research, as well as the methodological equipment of Soviet research workers, which has nothing in common with

the mechanistical and idealistical conceptions widespread among scientists in capitalist countries. Sarkisov's works have established the connection between afferent and proper-cortical neuronal processes. The scientist arrived at the conclusion that the channel leading to the afferent-cortex conveys impulses through extremely delicate processes—the minute points of the dendrons. These are exceptionally sensitive processes which change considerably during any action upon the vascular system of the brain and the cerebral tissue. The multiformity of the delicate mechanisms of the cortical structures is new proof of the absolute worthlessness of the viewpoints of narrow localisationists and equipotentialists in the teachings on the localisation of functions in the cerebral cortex.

In a paper on the physiological foundations of psychopathology, M. Gurevich, member of the Academy of Medical Sciences of the USSR, stressed that psychic functions cannot be equalled to nervous ones. A study must be made of the temporary relations which form the basis of integration and disintegration in the human mind. Pavlov's principle of temporary relations can be applied both to psychopathology and to phenomena of disturbed relations. This principle is also applicable to the process of the restoration of relations—reintegration. M. Gurevich expressed the opinion that acute psychoses are reversible processes, caused only by disturbances of the neuronal relations which are the basis of disintegration.

From the point of view of Professor A. Shmaryan, the pathogenesis of psychoses is based on three main factors: local or systemic, general-cerebral, and general-somatic. Each case of psychosis, even one with a clearly local cerebral affection, requires not merely a knowledge of the purely anatomical picture, but, at the same time, an understanding of the general pathogenetic nature of the development of the psychosis is imperative. A. Shmaryan considers that local affections of the brain do not result in a clearly-expressed picture of psychosis. In the opinion of this scientist, general-cerebral and general-pathogenetic factors must be added to the local affection before psychosis arises.

V. Gilyarovsky, member of the Academy of Medical Sciences of the USSR, and chairman of the Congress, pointed out that the chief factors of psychopathology can be understood from the point of view of the materialistic conception of the role of the environment. Already the great Russian scholar, Lomonsov, noted that sensations, feelings and ideas were the product of the influence exercised by the physical world upon the functional activity of the sensory organs and the brain. This relates wholly also to psychopathology. The radical questions of general psychopathology—hallucinations and delirium must be critically reconsidered.

Questions of criticism of present day theories on general psychopathology formed the subject of a report by Professor A. Edelstein, who dealt with the acute ideological struggle of the forces of progress and democracy against reaction in science. In studying the brain, which is the most complicated organ in the whole of the human organism, and psychic effects, neuropathologists and psychiatrists come into closest contact with philosophy, with such of its problems as cognition, reasoning, sensation, perception. Present day psychiatry in the U.S.A. and other capitalist countries is permeated by idealistic trends: Neo-Kantism, Freudism, Bergsonism. Reflecting the growing reactionary tendencies in politics and culture, psychiatry in the U.S.A. is slipping more and more into the sphere of pseudo-scientific psychoanalysis. The American magazine, "Psychiatry", for instance, prints such articles as "Theosophical Occultism," "Witches and Psychiatry," and so forth. In the U.S.A., psychiatry has become the helpmate of obscurantism and the priesthood.

In the ensuing discussions, the delegates to the Congress emphasized that the elaboration of a purely scientific theory of neurology and psychiatry is possible only on the basis of the philosophy of dialectic materialism.

During World War II and in the post-war period, Soviet neuropathologists and psychiatrists have accumulated much experience enabling them to approach in a new light a number of questions of the pathogenesis and treatment of nervous and psychic disorders arising from traumas of the brain. The Congress devoted much attention to these problems. Analysing the neurological and psychopathological syndromes in hidden traumas. Professor D. Shefer pointed out that in such traumas, of the brain, the chief pathogenetic mechanisms were shifting of the mass of the brain, a blow of the brain against the skull-box, or of the cerebrospinal fluid against the narrowest passages in the ventricular system. The morphological changes are accompanied by changes in the local chemism and gas-metabolism, and by swellings and inflation of the cerebral tissue. Professor R. Golant spoke of the peculiar lapses of optical memory and special forms of aphasia which she and her assistants had observed.

In reports on air concussions and the origin of neurological and psychopathological syndromes accompanying them, A. Geimanovich and S. Krai stressed that in the clinic of air concussions, disturbances of speech and hearing predominate. These scholars consider that a definite relationship exists between an air concussion and the appearance of the syndrome of deaf-dumbness. Experiments and pathologic-anatomical data bear witness to disturbances in the correlation of the movements necessary for respiration and articulation, and in the automatism of respiration and its conception with the delicate movements of the speech muscles, and to affections of the peripheral receptors of the auditory apparatus, in severe cases, even of the auditory centre.

Interesting data on traumatic epilepsy and traumatic cysts of the brain were presented by A. Minadze, I. Strelchuk, L. Rokhlin, G. Perushin and

A. Trofimov. In the light of neurological, anatophysiological data, a number of delegates (P. Emdin, M. Rapoport, L. Lobova and others) dealt with the picture of different psychopathological disturbances arising during remote complications from open wounds of the brain, depending upon the localisation of the wound, the stage of the process, and the general reaction of the organism.

The papers presented to the Congress on the subject of brain traumas showed the great scope of research and observations conducted by Soviet neuropathologists and psychiatrists, the unified, comprehensive nature of their works, the close collaboration of Soviet scientists in elaborating highly difficult problems.

Among the questions on the programme of the Congress was that of somatogenic diseases of the nervous system. V. Gilyarovsky in his report dealt with the problem of somatic and psychic inter-relationship in the clinic. Professor I. Ravkin mentioned the permanent relation between certain pathophysiological mechanisms and psychopathological manifestations. Professor E. Krasnushkin spoke of the consciousness and feeling of illness in somatic ailments. The consciousness of illness is, in the opinion of the speaker, the final result of all the conflicts causing somatic diseases. It expresses a condition of the defence and adaptation of the individual to the process taking place in the organism. The consciousness of disease is determined by interoceptive signals from the diseased organism in the form of a "vague feeling" (Sechenov), and from the individual affected organs (Bykov). Pointing to psychoses which in a number of cases arise some time after the somatic disease has run its course, and subsequently develop according to their own laws, regardless of the original cause, Professor G. Sukharev submitted the conception of a "second disease" in the clinic of somatogenic psychoses.

The Congress devoted considerable attention to vascular diseases of the brain and the significance of hypertension in their pathogenesis. Detailed analyses were given of the clinics of hypertonic apoplexy, psychopathological disorders due to disturbances in the blood-circulation, and the pathological anatomy of vascular diseases. Professors A. Grinstein and B. Yegorov spoke of their experience in treating vascular diseases surgically (operations on the marginal trunk). By surgical intervention in cases of severe hypertension, the authors achieved successful results in the treatment of a great majority of patients; the blood pressure dropped, and the brain symptoms decreased greatly or disappeared entirely.

The papers devoted to therapy of nervous and psychic ailments (M. Sereisky, E. Popov, A. Frumkin, B. Akkerman, and others), and the ensuing debate showed that Soviet medicine had achieved very real successes in this direction, and that in a number of questions it had far outstripped the medicine of capitalist countries. Active methods of treating psychoses have become widely popular in the Soviet Union, they are applied not only in clinics and hospitals in the capitals, but in medical institutions throughout the provinces. Here, we have in view insulino-therapy, shock therapy, electro-narcosis and other methods, the efficacy of which has been proved not merely experimentally but also clinically—on thousands of patients.

The delegates to the Congress learnt of the results of the latest methods of applying surgical treatment for psychic disorders. According to the observations of professors E. Yegorov, A. Shmaryan, I. Babich, R. Golant and M. Goldenberg, these methods yield a good effect in severe cases where other means have proved ineffective. According to Leningrad data, more than two-thirds of the patients who left hospital were cured to such an extent that they were able to resume work.

Questions relating to penicillin treatment for neurosyphilis were also discussed.

Like former congresses of Soviet neuropathologists and psychiatrists, the Third Congress devoted much attention to questions of the organization of psycho-neurological aid to the population.

THE NUFFIELD FOUNDATION

The Nuffield Foundation, because of the munificence of the automobile magnate Lord Nuffield, has spent or promoted grants amounting to $8,500,000 for research in its first five years. In their third report, just published, the trustees welcome the increased support of the state for learning and research but think that this does not decrease the need of alternate sources of support if the democratic principle is to be upheld, that there should be room for more than one opinion and for more than one means of putting that opinion to the test. The foundation is supporting three university chairs of industrial health, one of child health and four schools of dentistry. It is also financing laboratory studies of the blood and of the physiology of learning in animals, as well as some important sociomedical inquiries. A remarkable one is into the nature and circumstances of the middle class, "the main repository not only of administrative and professional ability but also of our cultural capital." This class has in the past received far less attention than have the wage-earners. The work is to be undertaken by the London School of Economics with a view to studying not only how people rise and fall in our complicated caste system but also whether the prevailing conditions of life for the middle class are becoming too difficult. The difficulty certainly is mainly due to the confiscatory prolongation of taxation on the war level to finance the socialistic measures of the labour government.

A gift of $1,800,000 has been made to the Nuffield Foundation by Captain O. Bird, who has suffered from osteoarthritis for many years, for promotion of research into the prevention and cure of rheumatism.—*J.A.M.A.*, **138**:984, 1948.

CORRESPONDENCE

[The Editor is not responsible for any views expressed by contributors]

AYURVAIDIC REORGANISATION COMMITTEE, U.P.

Sir,—The report of the Reorganisation Committee (set up by the U.P. Government) on the Ayurvaidic and Unani Systems demanding the Government "to declare immediately that henceforth all expenditure be directed towards expansion of medical and health facilities through the Ayurvaidic system" and to divorce the existing allopathic institutions to the care of philanthropic persons only, to whom Ayurvaidic institutions were hitherto left, is quixotic, chauvinistic and a disorganising judgment, bereft of a reorganising spirit but full of ruinous jealousy.

The plea advanced is that allopathic system is not suited to peoples "of different mental and physical make up, temperament, habits, *sentiments* and modes of living". When we consider the world-wide spread of allopathy in all the continents of the world the acceptance of these factors, interfering essentially with our remedial measures looks vain and false. The variations of these factors are noticeable even in individual persons of every country and they are to be encountered by proper selection of the drugs and their doses according to the sympathetic and parasympathetic understanding of the constitution, and temperament of the individual, determinable by certain intricate examinatons, and from the proper sorting of the patient's complaints, by skilled physicians of any school, as otherwise every school of medicine shall be as foreign to the patient as the allopathic school is considered to be. Happily for the physician, no drug ceases to produce its essential effects owing to the variations of these factors.

We often confound to establish the separate identity of a school of pharmacopeial differences. If this is to be relied upon then surely Ayurvaidic school has no antiseptics, hypnotics, analgesics, anæsthetics, antimalarial drugs, antisyphilitic drugs, antiamoebic drugs, vaccines and sera, endocrine glandular preparations, vitamins, sulfa drugs, penicillin etc. comparable with ours. The separate identity of a school is to be based on its teachings of ætiology, pathology, physiology, symptomatology, diagnostic methods etc. of the school, and for these the Ayurvaidic school is already depending on the allopathic teachers.

The committee wants to modernise the Ayurvaidic system and wants modern equipments also (microscope, X-ray, A.P. instrument, electrocardiogram etc. and surgical instruments). What will it mean? It will mean that after some time the Ayurvaids shall automatically reject their own characteristic theories and shall willy nilly accept our modern theories of infection, immunity, metabolism and the teachings of modern endocrinology, and dietetics etc. After this sure end there shall remain no difference between a vaid and a doctor. Frankly the demand of the committee aims at with false patriotic fervour, the retreading the well-trodden high roads of medicine and at digging the Ayurvaidic graves in the hope of finding some treasures of thtikhauem in the rejected ruins which to-day command only a few pilgrims. Even the advocates of these schools are not always their adherents for their family needs. In the modern Ayurvaidic institutions not only the anatomist, the physiologist, the pathologist etc. are allopaths, they have also to depend on foreign scholars for their research. While escorting me and showing me with vain brags the research laboratory of the Tibya Medical College at Delhi my Hakim escorter left me with anguish, when I asked him "Hakim Saheb, what is yours in this laboratory You do not know even the names and use of the instruments in the laboratory. It is that modest arduous skilled doctor Siddiqi who is doing all that for you. He can boast for the research done in your institution, not you", I was also shown a ticket of some patient by Dr. Naris Abbas in which Hakim Ajmal Khan had asked the doctor to examine the stools of the patient and to inject emetine, if the stool contained amoebae or their cysts. The doctor told that when they work systemetically they realise their drawbacks.

Another plea advanced by the Ayurvaidic Reorganisation Committee against allopathy was that this school was too costly. I wish to tell the members of the committee that after coming to the modern level Ayurvaidic school shall also become equally costly. The trend is evident even now. Ayurvaidic and Unani medicines now sold in the form of elixirs, tablets etc. are being sold with profits out of all proportion to their cost. Their manufacturers are mimicking the western manufacturers. Allopathy can be made cheaper by checking corruption in the profession. No practitioner should be allowed to have business relationship with patients. Their loot should be controlled. Disease does not justify a differential treatment for the rich and the poor and to give to the poor villagers what we would not give to the rich will be hitting at the productive economy of the country.

When I was a medical student Col. Sprawson used to say to his assistant "I do not think student X should pass this year. He is too raw and I do not want my students to be let loose like wild wolves on their patients". The patrons of the Ayurveda speaking of modernisation of the Ayurvaidic school should learn a lesson from this anecdote. I am etc.

BHOLANATH SHARMA, M.B.B.S.,

Moradabad.

Moradabad, 6-12-48.

SPRUE SYNDROME

Sir,—In your issue for October, 1948, Lt.-Col. Karamchandani has answered certain queries on Sprue Syndrome.

Few will agree with him that sprue passes through the four phases or stages as he calls them and describes them. The picture may be good enough for a fanciful description but is not commonly met with in clinical practice.

Sulphaguanidine is known to be effective in bacillary dysenteric diarrhoeas but it is not understood how it carries a patient of sprue from the jaws of death through remission to recovery as claimed by him.

I did read and have re-read his paper published in the *Indian Medical Gazette*, Vol. LXXXI No. 1. It has left me as unconvinced now as it did before of the accuracy of his diagnosis of the cases labelled sprue or sprue syndrome by him. To me it appears that they were a collection of diarrhoeas of all sorts. If Rogers and Megaw have said that any unexplained diarrhoea of more than 10 days' duration should be treated as sprue provided amoebic disease is excluded they and Manson Bahr have laid stress on the fat content of stools and the proportion of neutral fat to fatty acids therein in sprue, but Colonel Karamchandani seems to attach little importance to that.

We do "recognise and diagnose diseases after death and post-mortem" but when we do that we do not brush aside the report of the pathologist. He claims to have established the missing knowledge of pathology of sprue and yet he says: " What does it matter if the pathologist did not label it sprue". If this will not make confusion worse confounded what else will it do?

He may have carried with him "the gathering of over one hundred medical Pundits of the Indian Army" but if I am not mistaken he failed to carry with him a bigger gathering of civilian medical Shudras when he read a paper on this subject at the All-India Medical Conference at Madura in 1946. I am etc.

A. CHAND.

Green View,
Simla, 21-12-48.

MEETING OF THE CENTRAL COUNCIL

Sir,—It was my first occasion to attend the Central Council Meeting of The Indian Medical Association in December 1948 at Calcutta. Attendance of the Members from various branches was fairly good and showed that Members were finding interest in the affairs of the Association which is a good omen. In such a meeting of the learned profession I expected calm and dignified atmosphere; but at least to my mind I failed to find it. Some members were very impatient to give vent to their expressions on every item which, as was natural, were not well thought out, were many a time out of order and were not to the point. I remember one member talking on every item not knowing himself what he was saying and without giving heed to the Chairman's request to sit down. I would remind my friends that there are other fellow members who have equal right to speak and express their views. We must be disciplined to respect the Chair and the Chair should see that every member who wants to speak is given opportunity to do so. At one time there was so much digression from the subject under discussion that an unpleasant situation arose on account of the irrelevent and unfair expression of views. Ill wind blows no good to any body and that is what happened on that occasion.

Without referring to many subjects which were discussed, I would focus attention of all members of the Association on the question of approaching the Government for monetary help for delegations to attend Conferences in foreign countries. It should be a definite policy of the Association not to seek funds from any outside agency. If the Association seeks money from any agency that agency will naturally dictate terms and will interfere with the free will of the Association. Freedom of will and action is the most sacred and precious right which nobody will like to sacrifice for some paltry sum. Association should be able to raise separate fund for sending delegations.

There should be a rule that every member must bring credentials with him when he attends the Central Council Meeting. Credentials should show date of election of the member to avoid awkward situation.

My remarks are not made to castigate any member, but are made with the good intention of improving the tone of our meetings. I am etc.

P. S. GUPTA, CAPT., M.B.B.S.,
Nasik.

Nasik, 10-1-1949.

MAHARASHTRA & KARNATAK PROVINCIAL MEDICAL CONFERENCE

The 10th Maharashtra & Karnatak Provincial Medical Conference will be held at Kolhapur on the 7th, 8th and 9th of May, 1949 under the auspices of the Kolhapur Medical Association, branch of the Indian Medical Association.

There will be a Scientific Exhibition of surgical, medical and and allied products.

For further information please write to the Hon. Organising Secretaries. (Dr. Nagaonkar's Dispensary, Mahadawar Road, Kolhapur.)

CURRENT MEDICAL LITERATURE

The Mystery of the Eosinophil

An increase in circulating eosinophils is a feature of number of disorders which otherwise appear to have little in common. There are groups of conditions, such as allergic diseases of all kinds, parastic infestations, and cutaneous eruptions, in which we can at least say that sensitization, a metazoan parasite, or a visible skin disease links the group together. But outside these categories come a number of other conditions which appear to have nothing to do with three main groups. One of these is lymphadenoma: enlargement of lymph glands with eosinophilia nearly always leads to the diagnosis of that disease. The eosinophilia may be very marked indeed and extend to 50 per cent or more of the total leucocytes, themselves abnormally increased. Some have felt that this implies an allergic background, and attempts apparently unsuccessful, have been made to prove sensitization by intradermal inoculation of lymphadenomatous material. It is probable that in this disease the eosinophilia in the blood is the result of an overflow from the eosinophil deposits in the affected lymph glands, and that it is, therefore, analogous to the lymphocytosis in lymphatic leukaemia. Eosinophilic leukaemia may be considered as a disorder linking the true leukaemias and lymphadenoma, and lymphadenoma should be looked upon as one of many possible forms of malignancy in an organ with many functions and an eventful embryonic career.

Sometimes, however, eosinophilia with enlargement of lymph glands occurs in serum sickness and may be confusing. The presence of heterophilic antibodies to sheep red cells differentiates the two conditions—the test for these is so unpredictable and apparently irrational that it recalls some of the methods of mediaeval medicine in its more esoteric phases.

Allergic eosinophilia is most variable in its appearance. Many patients with severe asthma have no eosinophilia; on the other hand, there may be marked eosinophilia in patients who react acutely for the first time to certain drugs or foodstuffs.

Symptomless eosinophilia is most often due to metazoan parasites, and in certain parts of the world where helminth infestation is universal eosinophilia is equally common. In the tropical belt of Africa infestation by *Filaria perstans* is both symptomless and practically universal, at least in some areas, and the eosinophils may amount to 70 per cent or more of the circulating leucocytes. It should be remembered that amoebiasis does not cause eosinophilia—protozoa never evoke a response which is essentially metazoan. For some time to come helminth infestation must continue to be carefully excluded in adult males with eosinophilia, particularly in those who, interned in Japanese prison camps, so commonly contracted hookworm and *Strongyloides* infestation.

A further condition commonly associated with eosinophilia is periarteritis nodosa. This disease is to-day recognized to be more common than was once believed, and a proportion of the cases recover. Unless a biopsy is possible on a skin nodule the diagnosis of the condition must always be a guess; but eosinophilia is commonly encountered, and where albuminuria, fever, and eosinophilia are found together this disease must at least be considered. The contemporary view is that the condition is allergic, and the eosinophilia certainly gives this some support.

Of recent years there have been separated certain other conditions, all rare, in which eosinophilia is present in tissues or circulating blood and where some authorities have thought it possible to define clinical entities. One such condition is eosinophilic granuloma of skin, detailed studies of which have recently been published. (Weldman—*Arch. Dermat. Syph.*, **55**:155, 1947). Clinically the disease is stated to be chronic and usually self-limited condition in which doughy, firm, reddish-brown tumours form in the skin. The diagnosis is essentially a laboratory one, since eosinophilia of the order of 50 per cent is present in the circulating blood and also in the actual lesions. The condition is strikingly similar histologically to periarteritis nodosa, since the lesions occur in relation to small blood vessels and perivascular tissue. Allergy has also been confirmed in some cases; for example, a *Trichophyton* was grown from the feet of a patient, and trichophyton extracts gave positive intradermal reactions.

A much disputed eosinophilic disorder of the lungs was described by Loffler in 1932, and a similar condition, commonest apparently in India, is known as "tropical" eosinophilia. A survey of the latter condition has recently been made by Joseph (*Indian M. Gaz.*, **81**:512, 1946), who considers the two disorders distinct. But in certain cases such as that described by Perlingiero and Gyorgy (*Am. J. Child. Dis.*, **73**:34, 1947) infestation with roundworms has been present. Indeed, so many types of worms pass through the lungs at one stage of their life cycle that pulmonary symptoms due to their presence are inevitable. Very definite proof that a parasitic infestation is absent must be demanded before accepting these disorders as new entities. The discovery of mites in the sputum of patients must be accepted with abundant reserve. Entomologists tell us that their peace of mind is constantly being undermined by reports of mites in sputum, urine, or fæces. The truth is that mites are everywhere and easily fall into containers later filled with pathological material.

Eosinophilic granuloma of bone is a much more distinct entity. It was first described by Finzi in 1929, and something under fifty cases have been recorded. It is now generally agreed that the condition is one stage in the development of a disturbance of lipoid metabolism, and that the cumbersomely named Hand-Schuller-Christian disease is essentially the same disorder at an earlier stage. Other conditions in which tissue or blood eosinophilia may be present are numerous, but in most of them the eosinophilia is erratic and of most uncertain significance. In the whole gastro-intestinal tract, for example, acute inflammation is often eosinophilic; in widespread secondary malignant deposits blood eosinophilia has been recorded, but is not the rule; eosinophilia in blood and tissues occurs in some cases of radium sickness; and on occasion eosinophilic pleural effusions are found which appear to have no common aetiology or prognostic significance.

There is, in fact, no apparent link between all the varied conditions in which eosinophils are a prominent feature. But it is worth remembering that ignorance about the function of all other leucocytes, except the polymorph, is as great. No one has suggested what function a basophil cell or a monocyte may be expected to carry out. Lymphocytes amount to 40 per cent of circulating cells, yet few haematologists would like to be dogmatic about their purpose. If the eosinophil is

a mystery, it is at least in good company.—*Brit. M. J.*, 1:939, 1948.

Pruritus Ani—A Biochemiophysiological Entity

Bacon and Hardwick (*J. M. Soc.*, New Jersey, 44:446, 1947, Ref. *Rev. Gastroenterol*, 15:792, 1948) write that the hypothesis that pruitus ani is not due to local pathologic changes alone but to other factors was advanced about fifty years ago.

Physiologic factors in the anorectal region include the perianal skin with the sweat gland-bearing area, the local blood and nerve supply, the complicated physiology of the end-products of digestion, from which secretions bathe this area.

The functional activity of these sweat glands in this area are very important. There are two kinds of sweat glands—the eccrine or ordinary and the apocrine, which are found only where hair exists and are situated deep in the dermis. The apocrine glands begin to function at sexual maturity, producing a secretion which has a higher pH than ordinary perspiration. This secretion exists in the folds of the skin and furnishes ideal culture media for many organisms. This secretion also contains an excess of carbohydrate which is increased by a diet high in starches and sweets. It is possible by a reduction in diet of carbohydrates and an increase in proteins to change the bacterial flora.

Histopathologic changes in the area consists of an acute, subacute and an exudative dermatitis, much like a chemical dermatitis.

Anorectal pathology must be excluded—such as intestinal parasites, fungus infection, fissures, etc.

Careful history and proctological examination, examination for fungi and parasites, culture of anal skin scrapings and estimation of pH of rectal mucosa are necessary. The pH of rectal mucosa is reduced by means of acid-ash diet, glutasin capsules (glutamic HCl and pepsin, gelatin suppositories of beta-lactose. Local care of pruritic zone is important. Use of tissues or cotton saturated with boric acid after evacuation. The area is kept clean and dry with boric powder. Mercurochrome is applied daily to area. Soap or toilet paper is not used. If no response to this regime, condition should be treated from an allergic standpoint.

Amebiasis and Chronic Cholecystitis

In 500 cases of intestinal amebiasis, Professor Felicio Cintra do Prado of Escola Paulista de Medicina found 11 cases in which there was a prevalence of symptoms generally attributed to disturbances of the biliary ducts. The patients showed steady or intermittent pain in the hepatic region, tenderness over the vesicular area, nausea before breakfast and dyspeptic pain caused by foods, especially fatty foods. Cholecystography and duodenal intubation did not reveal any abnormality in these patients; feces, however, contained Endameba histolytica, and the apparently vesicular symptoms disappeared with the specific antiamebic treatment. Such cases are due to general toxic manifestations acting sporadically on the vesicular functions and, perhaps, in some cases to colitis predominating on the hepatic flexure, according to Professor Prado—*J.A.M.A.*, 138:985.

Thymine, Folic Acid and Vitamin B_{12} in Nutritional Macrocytic Anaemia, Tropical Sprue and Pernicious Anaemia

Spies and others (*Lancet* 2:519, 1948), write that a comparative study of thymine, folic acid, and vitamin B_{12} has been made under controlled conditions on selected patients with macrocytic anaemia in relapse. One patient with pernicious anaemia, one with nutritional macrocytic anaemia, and one with tropical sprue were each admitted three times to the hospital and given a diet free from meat and meat products. Base-line determinations were made on each admission. Each compound produced a blood response and a definite clinical improvement.

The fact that three distinct chemical compounds have proved effective in each of three distinct syndromes suggests that we may learn a great deal about the pathogenesis of these diseases.

From these and other studies by the authors it appears that several thousand times the weight of thymine is required to produce a response similar to that produced by folic acid, and that several thousand times the weight of folic acid is required to produce a response similar to that produced by vitamin B_{12}. These findings suggest that vitamin B_{12} is by far the most potent antianaemic substance known.

Lipotropic Factors in Cirrhosis

Sellars and Best (*Brit. M. J.*, 1:1012, 1948) from the Banting and Best Department of Medical Research, University of Toronto, write that young adult rats in which a moderate degree of cirrhosis had been produced by the administration of carbon tetrachloride were placed on diets containing different amounts of the following lipotropic agents; choline, methionine, protein (containing methionine), and inositol.

None of the animals receiving only a basal hypolipotropic ration showed improvement in the cirrhosis. Deposition of fat in the liver increased, degenerative renal lesions appeared, and six of the seven rats in this group survived less than three weeks.

When adequate amounts of pure choline chloride or dimethionine were added to the basal hypolipotropic diet a remarkable improvement in the gross appearance of the livers was noted within two or three weeks. After two or three months of this treatment the livers appeared normal, and on microscopical examination special stains were usually required to demonstrate any abnormal deposition of fibrous tissue. The processes by which this fibrous tissue may disappear have been discussed briefly.

A high-protein diet, containing 35% protein but low in methionine, was not as beneficial as a ration containing 20% of similar protein to which adequate supplements of choline or methionine had been added.

A high-potein diet which contained an adequate amount of naturally occurring methionine produced results as favourable as those which were secured when suitable amounts of choline or methionine were added to diets of lower protein content.

While the experimental evidence indicates that the presence of the lipotropic agents is essential for the repair of the

damaged liver under the conditions of the experiments, it does not suggest that the addition of choline or its precursor, methionine, to diets already containing adequate amounts of these factors will enhance the therapeutic effects unless some interference with the absorption or action of the liptropic agents exists.

No evidence has been secured that inositol exerts a favourable effect on experimental cirrhosis.

On the basis of the experimental findings it is suggested that the favourable clinical results which have been obtained in patients with liver damage when an effective therapeutic diet is provided may be attributable in large part to the lipotropic factors which the diet supplies.

Homologous Serum Hepatitis

Borenszrejn (*Lancet*, **1**:941, 1948) from an analysis of a series of 226 cases of hepatitis arising in patients under treatment for venereal disease observes:

Of the 226 cases 10 are excluded as not being due to a syringe-transmitted virus.

Syringes and needles washed in water, kept 3 min. in 5% carbolic acid or eusol 2% and then boiled 20 min. can be considered to be completely sterilised and free from contamination with the virus of hepatitis.

Homologous serum hepatitis is apparently transmitted by inoculation of an infective agent into the blood-stream at injection or blood test.

Homologous serum hepatitis is an infective disease due to a virus. Arsenic and protein deficiency may have a secondary effect in worsening the condition of the patient, but they cannot be incriminated as causal agents.

Homologous serum hepatitis is transmissible to rabbits

Sugar Tolerance as a Factor Producing Symptom Complex Simulating Peptic Ulcer, Neuro-circulatory Asthenia and Psychoneurosis

Peskin (*Am. J. Digest. Dis.*, **15**:92, 1948) gives in the following lines the summary of his observations:—

Four cases are presented in which vague symptoms of a bizarre character were experienced for four years. In some, there is a family history of similar complaints.

These symptoms were: nervousness, palpitation, apprehension, weakness in the legs, tremors, excessive perspiration, mental dullness and hunger pains relieved by food.

The symptoms were aggravated or precipitated by physical effort and were prevented or relieved by eating and rest.

The similarity of the group of symptoms, to symptoms associated with peptic ulcer, neurocirculatory asthenia, or psychoneurosis is discussed.

The disclosure of the true cause for these symptoms by a study of the sugar tolerance, suggested itself from the similarity of these symptoms to those of hypoglycemia.

Study of the blood sugar level at which symptoms of mild hypoglycemia occurred, revealed that these patients displayed symptoms at a relatively high sugar level. The implication of this observation is discussed.

Confirmation of the observation that these patients' symptoms are due to relative hypoglycemia, was revealed by reproduction of the same symptoms with insulin and exercise. At a relatively high blood sugar level (88 mgms. per 100 c.c.) one patient began to have symptoms as tremor, air hunger and a peculiar discomfort in the pit of his abdomen. More severe symptoms were evident at 74 mgms. of blood sugar. A disappearance of symptoms took place with the administration of orange juice.

The value of a high fat and high protein diet in the prevention and relief of this metabolic disturbance is discussed as is the physiologic principle upon which this treatment is based.

The practical value of the search for this entity in such obscure diseases as neurocirculatory asthenia, psychoneurosis, and peptic ulcer syndrome without positive x-ray findings, is discussed.

The role of the liver and thyroid efficiency in the maintenance of a so-called normal sugar tolerance is mentioned. These patients disclosed mild liver and thyroid dysfunction. No attempt has been made to discuss the bearing of these findings on the underlying carbohydrate tolerance.

The concept that mild symptoms of hypoglycemia may appear at a relatively high sugar level is stressed.

The author maintains that in citing these cases, he wants to provoke the medical profession into considering the role of glucose tolerance and relative hypoglycemia when confronted by an obscure case presenting a symptom complex identical with peptic ulcer, neurocirculatory asthenia, and psychoneurosis. It is hoped that a further study of this condition will reveal its frequency and its relation to the aforementioned symptom complexes.

Nutrition in Cardiovascular Disease

Peete (*Geriatrics*, **2**:213, 1947, Ref. *Rev. Gastroenterol.*, **15**:93, 1948) writes that recent advances in nutritional studies have led to greater understanding of the dietary deficiency states, especially with regard to vitamins, proteins and minerals. Experience shows that most pepole tend to form fixed dietary habits. An accurate appraisal of the patient's diet should be made from a list of his food eaten over a two week period. A very common form is low-protein intake leading to inadequate antibody formation with lowered body resistance.

Inadequacy in nutrition may produce disturbed physiological reactions without pathological evidence of disease, *e.g.*, on a starvation or low calorie diet, although diet is balanced, the pulse is slowed, blood pressure lowered and B.M.R. below normal while on a high calorie diet or obesity, pulse is increased, B.P. elevated, and B.M.R elevated. Thus, since obesity increases the work of the heart, reduction in weight reduces metabolism, improves pulmonary ventilation by lowering the level of the diaphragm and reducing the size of the capillary bed and lowers the B.P. The heart muscle itself shows no changes, except in extreme deficiency states.

A few points to be kept in mind. Nitrogen metabolism is directly dependent on calcium metabolism and calcium metabolism on adequate vitamin D intake. Carbohydrate metabolism is dependent on thiamin chloride and niacin. while many of the vitamins are synergistic in their action.

Some of the specific changes affecting the cardiovascular system are:

1. Lowered blood sugar or overdose of insulin may precipitate an attack of angina pectoris. In these cases vitamin B and niacin should be given with carbohydrates.

2. The wet form of beri-beri affects the heart and vascular system due to thiamin deficiency and associated hypoproteinemia.

3. Long continued heart-failure with c.p.c. of liver and G.I. tract produces an inability to absorb thiamin, proteins and glucose, thus producing a deficiency state making their condition worse.

4. EKG changes produced in thiamin therapy. These changes consist of low-voltage, iso-electric or inverted T wave, increase in QT time and ectopic beats.

5. EKG changes in pellagra were low upright T waves in all leads or depression or flattening of the T or ST segments in two or more leads. These changes reversed themselves in 6-7 days treatment with 350-500 mg. niacin daily.

6. EKG changes in calcium deficiency were prolongation of the QT time or contraction time of the ventricle, varying from 0·25 sec. for 120 rate per minute to 0·45 sec. when the rate dropped to 45 per minute. These changes were altered with large doses of calcium and vitamin D.

7. Arteriosclerosis is not influenced by high cholesterol intake, as was formerly thought.

8. Rheumatic fever is benefited greatly by rest, high protein, high mineral and high vitamin diet, together with ultra-violet and sun-bathing.

Cholesterol Metabolism in Acute Coronary Thombosis

Morrison and others (*Am. J. M. Sc.*, **216**:32, 1948) write that a consecutive unselected series of 200 patients with acute coronary occlusion was studied for blood cholesterol and cholesterol ester levels within 48 hours after hospital admission.

In 68% of 75 patients under 60 years of age with proven acute coronary occlusion hypercholesterolemia was present.

In 52% of 125 patients over 60 years of age with proven acute coronary occlusion a normal cholesterol level was found.

Coronary thrombosis in patients under the age of 60 is frequently associated with hypercholesterolemia and disturbances of cholesterol metabolism.

Vitamin E Deficiency and Vascular Disease

Shute and others (*Surg. Gynec. & Obstet.*, **86**:1, 1948, Ref. *Practitioner*, **160**:252, 1944) write that deficiency of vitamin E may play a part in the genesis of vascular diseases as is indicated by the results obtained in a series of cases of vascular disease, including thrombophlebitis, indolent ulcers of the legs, gangrene of the extremities, and thromboangitis obliterans, with alpha tocopherol. The dosage employed was from 200 to 300 mgm. daily, by mouth, except in acute cerebral thrombosis, when the drug should be given parenterally in order to procure early saturation of the patient to minimize the risk of brain cell damage. It is stressed that the vitamin E employed must be alpha-tocopherol, and no inorganic iron should be administered to the patients. In three cases of thrombophlebitis, one ante-partum and one post-partum, 200 to 300 mgm. of alpha-tocopherol daily by mouth resulted in clearing of the condition in an average of four weeks. In a case of ulceration of the leg of nineteen years' duration, in a sixty-three year old man, 250 mgm. of alpha-tocopherol daily by mouth resulted in complete healing in ten weeks. A case of dry gangrene of the feet and legs, in a man of seventy-four, responded well to 300 mgm. of alpha-tocopherol daily by mouth, and just over one month later both feet were healed and the patient began to walk. On admission this case was regarded as one for amputation of both legs. Two cases of thromboangitis obliterans are also recorded, in both of which good results were obtained. It is stated that although the group studied was small the results of the therapy were encouraging, and may indicate a valuable addition to the prophylaxis of vascular diseases. It is necessary to continue the alpha-tocopherol at a high level after healing has been obtained, as in some cases relapse occurred when treatment was stopped.

The Importance of Occult Blood in the Stool

Paul and Hamilton (*Am. J. Digest. Dis.*, **15**:26, 1948) emphasize the importance of digital examination of the rectum and a test for occult blood as a routine part of the physical examination, even when there are no definite gastro-intestinal symptoms. For the occult blood test, the washings from the gloved finger used for rectal examination are employed. Reagents that have been employed for the test for occult blood have been difficult to handle, but recently a tablet using orthotolidin as the reagent (Hematest tablet) has become available, which simplifies the procedure. For tests with this tablet a drop of the washings from the gloved finger is placed on a small piece of filter paper, the tablet is placed on this moistened filter paper and two drops of water are permitted to flow over the tablet and down on the filter paper. The tablet is very sensitive for occult blood; a proportion of occult blood of 1:20,000 will give a blue colour within two minutes. Three illustrative cases are reported, showing the value of the digital rectal examination and occult blood test. In the first case, the patient showed definite anæmia, and had had only vague gastrointestinal symptoms; the test for occult blood was strongly positive; further x-ray and sigmoidoscopic studies showed ulcerative colitis to be the cause of recurrent blood loss. In the second case, although there was no history of bowel disorder, the test for occult blood was positive and further diagnostic study showed a carcinoma of the rectum, which was successfully removed by abdominoperineal resection before any metastasis had developed. In the third case there was a history of constipation and vague abdominal symptoms for several years and gastric distress for one year, associated with a psychoneurosis. Physical examination was "essentially negative" except for the finding of occult blood in the stools. X-ray and gastroscopic examination showed a large ulcerating lesion on the lesser curvature of the stomach which proved to be carcinoma and inoperable.

Pyuria in the Diabetic

Rohrer (*J. Urology*, **59**:385, 1948) reports that in the examination of 2674 diabetic patients in the past twenty-five years, more than 10 pus cells to the high power field were found in 334 cases, or 12·3 per cent. In the same number of non-diabetic patients, the same degree of pyuria was found in only 201 cases, or 7·1 per cent. An analysis is made of

107 cases of pyuria in diabetics in which the infection was proved to be proximal to the urethra. The method of collecting the urine in these cases was either by catheterization or by voiding in two portions after cleansing the meatus. With the latter method, the first voided urine was discarded; the second portion was centrifuged, the sediment examined for pus and for bacteria with a gram stain); in most cases a gram-negative bacillus was found to be the causative organism. Of the 107 patients with persistent pyuria, 68 were referred to the urologist for further study. Cystoscopic examination was done in 52 of these cases. Cystitis and chronic pyelitis and pyelonephritis were the most common findings; there were 7 cases of carcinoma of the bladder. Operation was done in 12 cases, including transurethral resections in the 7 cases of benign hypertrophy of the prostate, and 2 nephrectomies. There were no operative deaths. All patients were given careful preoperative treatment, including adequate control of the diabetes. Adequate control of the diabetes is an essential factor in the treatment of all urinary tract infections. In cases of gross pyuria, it was found best to hospitalize the patient and employ an inlying catheter with frequent irrigation with a mild antiseptic solution and continuous catheter drainage. In the more recent cases, the use of sulfonamides, penicillin and streptomycin, on the same principles as in other urinary tract infections, has shortened the period of hospitalization and treatment. Mandelic acid in large doses and neosalvarsan intravenously are still of value against certain organisms. In upper urinary tract infections, especially in pyelitis, ureteral cathetrization and pelvic lavage with ½ of 1 per cent mercurochrome or silver nitrate (¼ to ½ per cent solution) has also proved of aid. In patients with diabetes who develop acute urinary tract infection some time after the diagnosis and treatment of the diabetes, there is a marked rise in blood sugar and increase in the insulin requirement at the onset of the infection. The sooner the acute infection is treated and controlled, the sooner the blood sugar and insulin requirement decrease. In the cases in this series, the operations performed on the urinary tract did not aggravate the diabetes. In one case of unilateral tuberculosis of the kidney and epididymis, removal of the kidney and epididymis resulted in a drop in the blood sugar and insulin requirement and in much easier control of the diabetes.

Treatment of Persistent Colon Bacillus Infections of the Urinary Tract by Sulfasuxidine and Streptomycin

Crowley and O'Conor (*Surg. Gynec. & Obstet.*, **86**:224, 1948) report the first use of streptomycin in the treatment of a colon bacillus infection of the only remaining kidney in a patient who had been on sulfasuxidine for three months with only slight improvement; 5 gm. of streptomycin were given over a period of six days; the urine rapidly cleared, sulfasuxidine was continued for four months, and the urine has been clear of pus and bacteria for six months. Since that time 23 patients with persistent colon bacillus infection of the urinary tract have been treated with a combination of sulfasuxidine and streptomycin. Sulfasuxidine was given for varying periods of time before, during and after the administration of 5 to 17 gm. of streptomycin; the usual dose of sulfasuxidine was 4 gm. daily. In 19 of these 23 patients the urine has been free from pus and negative to culture for periods of four months to fourteen months(in all but 2 cases, six months or more). In 2 cases, the urine became temporarily clear, but a relapse occurred when sulfasuxidine had to be discontinued; in 2 cases, negative cultures were never obtained with the combined treatment. The toxicity of sulfasuxidine is low and the drug can usually be given in large doses for long periods of time.

Causes of Globus Hystericus

Stinson (*J. Tennesses S.M.A.*, **60**:10, 1947, Ref. *Rev. Gastroenterol*, **15**:90, 1948) deplores the tendency to consider all patients with a lump in the throat as hysterical, especially if they are nervous or on the hypochondriac side. He divides globus hystericus into three categories, namely: (1) Sensations occurring as sequelae of organic conditions, usually inflammatory, such as tonsillitis or pharyngitis. (2) Poliferative lesions, such as polypus, cysts, tumors, calculi, or diverticula. (3) Neuroses usually initiated by some slight pathology.

He urges that every case of globus hystericus be considered of organic origin until proven otherwise by a careful and exhaustive study of the entire region involved. He is of the opinion that this condition is more often overlooked than found.

Severe Cardial Pain as a Prodrome in Idiopathic Epilepsy

Fischer (*Am. J. M. Sc.*, **216**:78, 1948) writes that two cases of idiopathic epilepsy are described in which the prodromata consisted of severe paroxysmal cardiac pain simulating true angina pectoris. In one case, though rheumatic aortic insufficiency and mitral stenosis and insufficiency were present, it was felt that these valvular lesions did not contribute to the angina pectoris syndrome.

It should be emphasized that severe precordial pain may be due not only to intrinsic disease of the heart or aorta, but also to abnormal states of the nervous system.

Triple Sulphonamide Mixture

Ledbetter and Cronheim (*Am. J. M. Sc.*, **216**:27, 1948) write that a mixture containing sulfadiazine, sulfamerazine and sulfathiazole in microscrystalline suspension has been studied with regard to absorption, excretion and crystalluria.

Adequate blood levels are maintained on the usual dosage schedule of from 2 to 4 gm. of total sulfonamides intially followed by 1 gm. every 4 hours.

The incidence of crystalluria is extremely low even though no alkali was administered in any form. In no case was it necessary to discontinue drug treatment.

The acetylation of the sulfonamides in both blood and urine seems to be noticeably reduced.

Efficacy of B.C.G. Vaccination

Malmors (*Brit. M. J.*, **1**:1129, 1948) gives in the following lines the summary of his observations:

The harmlessness of B.C.G. is established beyond doubt. If Wallgren's method is used and the vaccine in a dose of 0·05 mg. is injected strictly intracutaneously, large abscesses very seldom appear (0·8%). Small abscesses occur in about 7·8%. They heal, however, relatively soon and without giving any persistent lesions. In newborn infants abscesses occur much more rarely (2·3%) than in older children and in adults. Nor does B.C.G. vaccination involve any other unpleasant effects. Birkhaug's needle-puncture method cannot be recommended.

The newborn become tuberculin-positive after vaccination to the same extent as older children and adults, subsequently remaining positive for several years.

Of the 22,413 B.C.G.-vaccinated cases during the period 1942-7, only one developed tuberculosis—a pleuritis in a probationer nurse who was tuberculin-negative in spite of two B.C.G. vaccjnations.

In other places where B.C.G. vaccination has been employed to a great extent a definite impression has been made that it gives good protection against tuberculosis, although on account of the absence of controls this cannot be regarded as proved.

In earlier investigations published conjointly with Hedvall Malmors shows that pulmonary tuberculosis in adolescents often develops in connection with a recent primary infection. Several other Scandinavian investigators have arrived at a similar view. Hyge's investigation of a tuberculosis epidemic in a school would seem to have placed it beyond all doubt that B.C.G. vaccination can prevent a development of progressive pulmonary tuberculosis in the majority of cases.

B.C.G. vaccination of all newborn infants and the vaccination of non-reactors, first proposed by Heimbeck, ought for this reason to be utilized to the greatest possible extent.

Hormones in the Treatment of Obesity

Kunde (*Ann. Int. Med.*, **28**:971, 1948) writes that no hormones or gland products known to therapeutics at this time are necessary adjuncts in the treatment of any type of obesity, excepting hypothyroidism.

A high protein, low fat, low carbohydrate, *ad lib.* diet, supplemented with vitamins and minerals, and with no calculation of caloric values, and without the administration of any known hormones, results in satisfactory weight reduction in all known types of obesity.

Endocrine obesity is a term which is misleading in that it conveys to the obese patient a false idea, suggesting that his obesity is due to some specific endocrine glandular deficiency which can be corrected by substitution endocrine, or hormone therapy. This causes the patient to seek needless endocrine medication, whereas dietary measures and reeducation of his faulty food habits are the true solutions to correction of obesity.

Nasal Haemorrhage

Neivert, and others (*Arch. Otolaryng.*, **47**:37-45, 1948) studied 104 patients subject to epistaxis and found a high incidence among them of ascorbic acid and prothrombin deficiency. The concentration of ascorbic acid and prothrombin was normal in less than eleven per cent.

Gratifying clinical results were obtained with the administration of ascorbic acid and vitamin K. The authors conclude that vitamins C and K have a definite place in the management of nasal hæmorrhage.

Penicillin in the Post-Operative Treatment of Peptic Ulcer with Perforation and Appendicitis with Perforation

Brown and Andrus (*Ann. Surg.*, **128**:57, 1948) report basing on a study of 42 cases of perforated peptic ulcers and 97 cases of perforated appendices operated on at the Philadelphia Naval Hospital during the 18-month period between January 1, 1946, and June 30, 1947. Patients from the Veterans Administration and active duty personnel are included in the series. Since the vast majority of these cases were surgical emergencies, operation was performed by the surgical watch officer. This officer is usually a younger surgeon with experience comparable to that of a surgical resident or younger staff man in a civilian hospital.

—There has been no rigid standardization of surgical procedure. On the other hand the post-operative care in this series has been quite uniform throughout for each of the two groups of patients. In practically all of these cases the same ward medical officer supervised this care. With few exceptions penicillin was administered post-operatively. Although some of the cases treated early in 1946 and an occasional case treated later received a smaller dosage of penicillin, 100,000 units every two hours became the accepted initial post-operative dose.

Penicillin was maintained at this dosage level for days or even weeks in those cases in which the slightest indication of continuation of therapy persisted.

In a group of 42 ruptured ulcers there were two deaths; a mortality rate of 4·8 per cent. There were only two wound complications in the group, neither primarily infectious.

There were 97 perforated appendices in a total series of 815 appendectomies. There was one death; a mortality rate of 1 per cent for the ruptured appendices and 0·12 per cent for the entire group.—*U. S. News Letter.*

Surgical Aspects of Hyperparathyroidism

Black (*Surg. Gynec. & Obstet.*, **87**:172, 1948) reports on 63 per cent patients with proved hyperparathyroidism that were observed at the Mayo Clinic to the end of 1946. Some of these cases had been described previously.

The surgical problems associated with hyperparathyroidism, broadly considered, resolve themselves into the finding and removal of parathyroid tumors or the recognition and subtotal removal of hyperplastic tissue in cases of diffuse primary hyperplasia. The surgical difficulties have to do chiefly with the minuteness and varied locations of the parathyroid glands, and the small size of many of such tumors, and the fact that the tumors may be multiple.

In the 63 cases reviewed in this paper the disease was due to a single adenoma in 56 cases, to multiple adenomas in three cases, and to diffuse primary hyperplasia in four cases. The ages of the patients ranged from the second to the seventh decade. Complications of the urinary tract were more common and more important than osseous complications. The diagnosis was established with certainty in three cases in the absence of any complications, on the basis of the characteristic changes in the content of calcium and phosphorus in the blood and urine. Since the diagnosis can be made with complete certainty, exploration of the parathyroid glands is never indicated to establish the diagnosis, and the surgeon must accept the

fact that in every case of hyperparathyroidism one adenoma or more or primary hyperplasia is present.

The treatment of hyperparathyroidism is surgical. Adonemas should be removed completely and, in cases of diffuse primary hyperplasia the hyperplastic tissue should be excised subtotally, with the preservation of between 30 and 200 milligram of hyperplastic tissue. In more than 80 per cent of cases, the abnormal tissue may be found by dissection under direct vision through a cervical incision (cervical and posterior superior mediastinal dissection). A second operation, through a sternotomy incision, will be necessary in the remaining cases (anterior superior mediastinal dissection). Secondary dissection is more difficult and far less certain than primary dissection, so that every effort should be made at complete operation, both in identifying the parathyroid glands present and in designating those missing, at the first cervical dissection.—*U. S. News Letter.*

Typhoid Fever in Children in Kweichow

Kao (*Chinese M.J.*, **66**:391, 1948) gives in the following lines the summary of his observations:

An analysis of 126 cases of typhoid fever occurring in children under the age of 12 years is presented.

The incidence of typhoid fever among Kweichow children is 2·8 per cent. Fifteen per cent of the cases occurred in children under the age of 2 years. Three patients who had had one injection of typhoid vaccine suffered a milder form of the disease. The seasonal incidence of typhoid fever in Kweichow is highest in the summer.

The majority of patients were admitted with the chief complaint of fever, which was usually accompanied by poor appetite, constipation, cough, general malaise, headache and abdominal pain.

Rapid pulse, high fever, coated tongue, anorexia, and enlargement of spleen were the symptoms and signs most frequently observed. Rose spots were observed in only 19 patients or 14·2 per cent.

The diagnosis of all cases of typhoid fever was confirmed by blood culture, urine culture, stool culture and Widal test. The leukocytes numbered less than 5,900 in 49 cases or 38 per cent; 6,000-8,900 in 91 cases or 42 per cent; 9,000 and over in 26 cases or 20 per cent.

Fifteen cases or 11·9 per cent of the patients of the series developed bronchopneumonia. There were four deaths, with a mortality of 3·17 per cent. Eigty-seven cases (69 per cent) had constipation. Twenty-one cases had diarrhoea—proper diet, bismuth and calcium acetate usually checked this in three to four days.

There were three forms of typhoid fever: Duration from 11-25 days, 36 cases or 28·5 per cent; 26-35 days, 45 cases or 35·75 per cent; 36-133 days, 45 cases or 35·75 per cent.

In the differential diagnosis, the following should be considered: tuberculous meningitis, typhus fever, relapsing fever, and malaria.

The treatment is discussed.

Kerosene Poisoning in Children

Like all other volatile hydrocarbons kerosene (lamp-oil) is essentially a narcotic, producing cerebral depression and a more or less severe paralysis of the vagus and respiratory centre. It appears, however, that children who recover from the immediate injurious effect of accidentally swallowing kerosene may develop later lesions, both inflammatory and degenerative-inflammatory in the lungs, and degenerative in the myocardium, the liver, the kidneys, and the gastro-intestinal tract.

A recent analysis (Steiner—*Am. J. Child. Dis.*, **74**:32, 1947) of 35 cases of accidental kerosene poisoning in children divides them roughly into three groups, according to the predominating incidence of cerebral, pulmonary, and degenerative signs. The cerebral group showed marked drowsiness but very little evidence of lung involvement, and they recovered rapidly. The pulmonary group developed severe pneumonia, and recovered slowly. Children in the degenerative group also had severe pneumonia, but in addition developed signs of cardiac injury, persistent albuminuria with blood cells and casts, and, in some cases, hepato-splenomegaly and occult blood in the stools.

Whether aspiration of kerosene or its absorption from the gastro-intestinal tract is the more important cause of the pulmonary and organic lesions is still a matter of some uncertainty, but animal investigations (Deichman and others)—*Ann. Int. Med.*, **21**:803, 1944) have indicated that vascular damage resulting from absorption into the blood stream is certainly a factor in both.

In any case the treatment is to remove as soon as possible all traces of kerosene from the gastro-intestinal tract in order to prevent not only further absorption but also further injury to the mucous membranes. In the 35 cases referred to, emergency treatment consisted of copious gastric lavage with weak sodium bicarbonate solution, administration of cardiac stimulants, or penicillin to prevent secondary bacterial infection of the lungs, and of dextrose solution and oxygen to reduce the hazard of pulmonary oedema. All these children made a complete recovery, even the degenerative changes proving reversible and leading to no permanent damage.—*Brit. M. J.*, **2**:688, 1948.

Penicillin in Diphtheria

The following is the summary of the Report of a Sub-Committee of the Public Health Laboratory Service, England:—

Penicillin-sensitivity tests were carried out on 284 strains of *C. diphtheriae* isolated in different parts of the country. Most of the strains tested were two or three times as resistant to penicillin as the Oxford staphylococcus. Gravis strains of *C. diphtheriae* were more resistant to penicillin than intermedius, and intermedius were more resistant than mitis types.

Of 65 acute cases of faucial diphtheria treated with penicillin, 26 of 37 receiving a three-day course, and 23 of 28 receiving a six-day course, became free from the infecting ogranism within four days of the end of treatment. In 31 persistent diphtheria carriers penicillin treatment was followed by the rapid disappearance of the organism from the throat in only 13 cases.—Lancet, **2**:517, 1948.

Infantile Gastroenteritis with Oral Streptomycin

James and others (*Lancet*, **2**:555, 1948) write that streptomycin was given by mouth in thirty cases of infantile

gastro-enteritis. Its effects were most striking in the critically ill cases, in cases of recurrent diarrhoea and vomiting, and in neonatal gastro-enteritis. Vomiting ceased early, weight was rapidly gained, the appetite returned, the stools improved, and there was almost immediate improvement in the general condition

Streptomycin 2 g. by mouth in 7 days was given without producing toxic effects. It was palatable and well tolerated, even, where there had been copious vomiting. To maintain a constant bacteriostatic concentration, the total daily dose of streptomycin is dissolved in sterile water and an equal fraction is given immediately before each feed.

The administration of streptomycin by mouth does not obviate the necessity of treating parenteral infection, which may play a part in the causation of gastro-enteritis.

There is a danger that pathogens remote from the gut may be rendered streptomycin-resistant by the small amount of streptomycin that enters the blood-stream.

Streptomycin by mouth effectively eliminated *Proteus vulgaris* from the stools and was also effective in cases of gastro-enteritis where no pathogenic organisms were found.

Streptomycin by mouth shortened the course of gastro-enteritis to a considerable extent, the usual time of discharge from hospital being 9-14 days after the start of treatment, even in the very severe cases. This is a great asset in alleviating the pressure on beds and lessening the risk of cross-infection.

The early administration of streptomycin by mouth in gastro-enteritis may make it possible to omit a period of starvation and to give generous feeds throughout the illness.

Cancer in Children

Cancer, in general, is a disease of the elderly, but it sometimes appears in a child, and the doctor's philosophy and understanding may then be strained to the utmost. Often no cure is possible from the first, the miseries of the child are hard for parents to bear, and symptomatic relief may be temporary and incomplete. A small gleam of light is provided by Dargeon (*J.A.M.A.*, **136**:459, 1948) in a paper sponsored by the American Medical Association and the American Cancer Society. The importance of the subject can be gauged by the fact that in New York, in the three years 1942-44, "cancer and other tumours" accounted for 215 deaths in children against 291 for tuberculosis, and in the U.S.A. as a whole "cancer and allied diseases" was the third highest cause of death between 3 and 10 years, and the sixth at 10-14 years. The commonest sites for juvenile cancer are the bones, kidneys, eye and orbit, and the lymphatic and blood-forming organs; tumours may also arise in the nervous system, muscle, and other connective tissues. The detailed recognition and management of these different kinds of new growth are systematically described by Dargeon, and he emphasises the fact that although many of the tumours have an unfavourable prognosis from the beginning, this is not an invariable rule—for example, osteochondromas and giant-cell tumours of bone only become malignant with the advance of time; there have been several instances of children surviving for more than ten years after treatment for cancer of bone. Our general attitude toward so-called benign tumours, he thinks, should be revised without delay.

The universal desideratum is early and correct diagnosis, followed immediately by suitable treatment; the sooner surgical operations are done, the less mutilating they are likely to be and the better the chances of permanent cure. To secure quick recognition, Dargeon recommends that every child should be examined monthly during the first year, quarterly from 1 to 6 years, and every six months thereafter. Biopsy should be done at once on every swelling of non-traumatic origin as well as on those which, though following injury, have persisted unusually long; all potentially malignant growths, including melanomas, teratomas, dermoids, and neuromas, aught to be excised without delay. Even an atypical symptom-complex demands thorough investigation, for the cause may be a hitherto undetected neoplasm. The essential change required is that doctors examining children should keep malignant disease in mind as a possibility and not exclude it automatically on grounds of age.—*Lancet*, **1**:954, 1948.

Roentgen Treatment of Subacute Sinusitis in Children

Laing (*Radiology*, **50**:50, 1948) writes that children with an upper respiratory infection for more than five or six days should have nasal smears made to determine the presence of pus cells and eosinophils. A single radiograph of the sinuses is of diagnostic value.

In the past ten years the author has given roentgen treatment for sinus infection to more than 4000 children between the ages of one and thirteen years. 900 were selected for this study, showing varying degrees of maxillary and ethmoid sinus infection of the subacute type.

Three treatments over a period of 8 days with a total of 240 were given. X-ray factors for younger and older children are detailed.

71% of the 900 cases were cured after one roentgen treatment series.

15% showed moderate improvement. Repeating the treatment series in the remainder after 6 weeks' interval cured 55%. This gives complete recovery in 79% of the total group, a favourable result in 7% and temporary or no response in 14%.

Hufford reported that 56 children with hypertrophic lymphatic tissue causing eustachian tube block showed marked improvement or complete relief from deafness in 73 per cent of cases following roentgen therapy.

A. F. Rossitto reported comparable results in 600 cases of sinusitis.

Laing gives three treatments spaced over 8 days; the average dose is 80 r, making a total of 240 r as a series. Sulfonamides are not given during the treatment and he prefers not to give roentgen therapy to patients who have had a sulfonamide within the previous five to seven days.

The author has cures in approximately 80 per cent of the eustachian tube block cases.